The Art of Medicine

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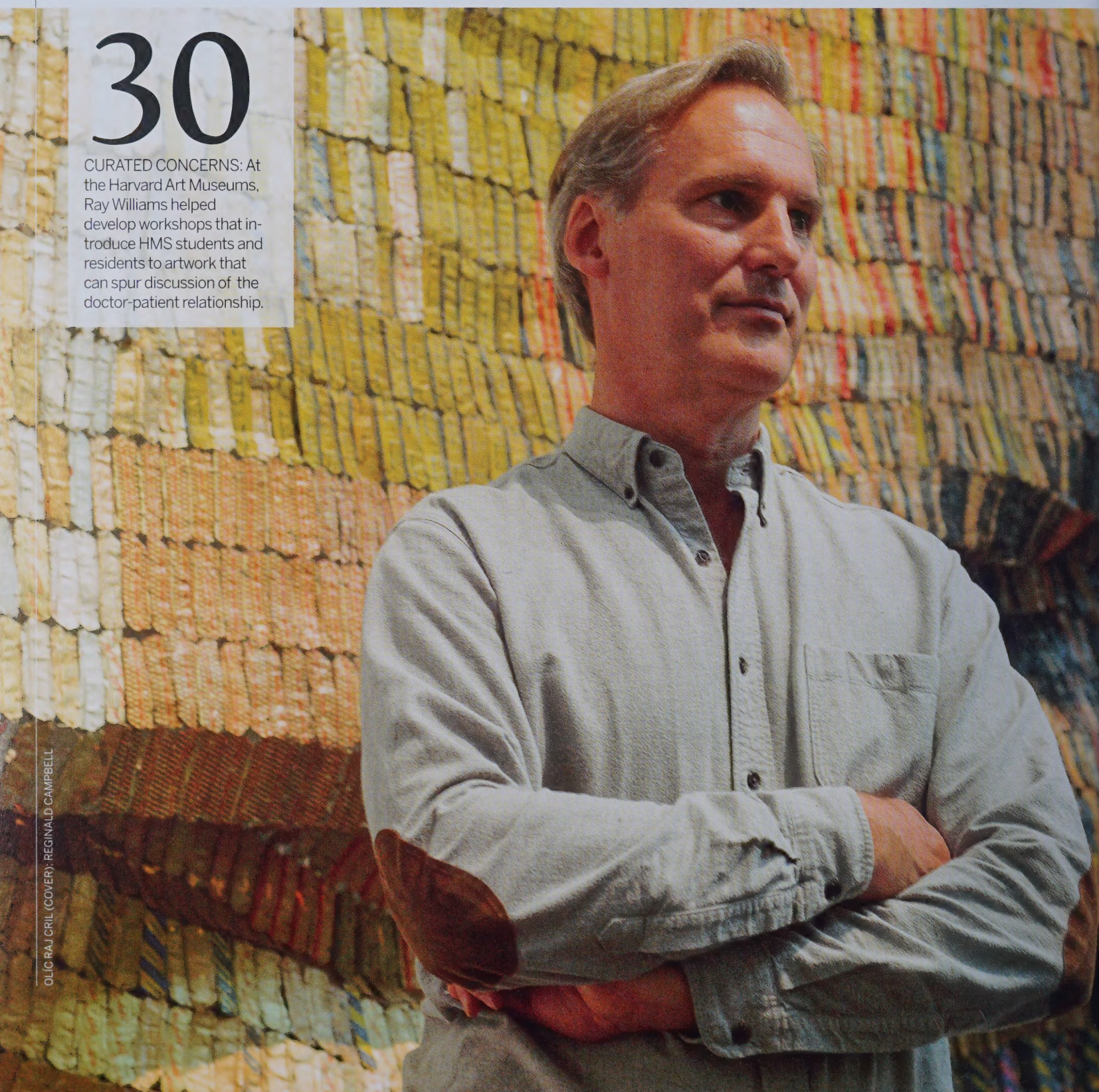

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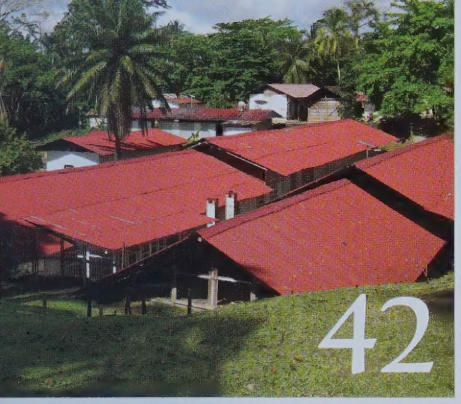

Special Report: The Art of Medicine

Feature

Departments

From the Dean

ART HISTORIANS TELL US of the strong connections between painters and physicians. The poet and physician John Keats, for example, had a close, creative relationship with the English portrait painter Joseph Severn, while Paul-Ferdinand Gachet was a physician to Vincent Van Gogh and the subject of his patient's now-famous painting.

Physicians themselves have often taken up the brush. The Russian physician Leonid Pasternak was a well-known portraitist, and father to novelist Boris; and Carl Gustav Carus—friend of Goethe, one-time physician to a king of Saxony, and author of *Psyche*, a book thought to have influenced Carl Jung—was a painter.

Carus was known for the scientific precision of his landscapes. Two of the people we feature in this issue of *Harvard Medicine*, an issue devoted to the art of medicine, are also known for their meticulous, empirical approach to their compositions. Warren and Lucia Prosperi have produced dozens of portraits of notable HMS clinicians and researchers, as well as large paintings and murals of landmark events in medicine.

Elsewhere in the issue, we appreciate the adeptness with which artists probe, even play with, our visual systems' responses to the hues, saturation, and luminance of colors. From a curricular standpoint, we consider how artwork taps the emotions and contributes to the observational skills of our physicians, residents, and medical students. We also describe how the work of an artist can captivate a physician in our tale of Harvey Cushing, Class of 1895, a twentieth-century neurosurgeon, and Andreas Vesalius, a Renaissance anatomist and artist.

When physicians and painters collect their thoughts on a patient or a painting, they're translating what they see, hear, and feel. Francis Peabody, Class of 1907, recognized this when, in his *The Care of the Patient*, he wrote: "What is spoken of as a 'clinical picture' is not just a photograph of a man sick in a hospital bed; it is an impressionistic painting of the patient surrounded by his home, his work, his relations, his friends, his joys, sorrows, hopes, and fears. ..."

We invite you to look and to savor.

Jeffrey S. Flier
Dean of the Faculty of Medicine
Harvard University

HarvardMedicine

Editor
Ann Marie Menting

Design Director
Paul DiMattia

Assistant Editor
Susan Karcz

Senior Graphic Designer
Jill Carrico

Contributing Writers
Michael Blanding, Haley Bridger, David Cameron, Jessica Cerretani, Bobbie Collins, Elizabeth Cooney, Suzanne Day, Elizabeth Dougherty, Stephanie Dutchen, Elissa Ely, Nancy Fliesler, Michael LaCombe, Kelly Lawson, Jeffrey Mifflin, Jake Miller, Bonnie Prescott, Amy Roeder, Emily Wilson, Savannah York, Sarah Zobel

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Phone: 617-432-7878 • **Fax:** 617-432-0446
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Mail: 107 Ave. Louis Pasteur, Boston, MA 02115
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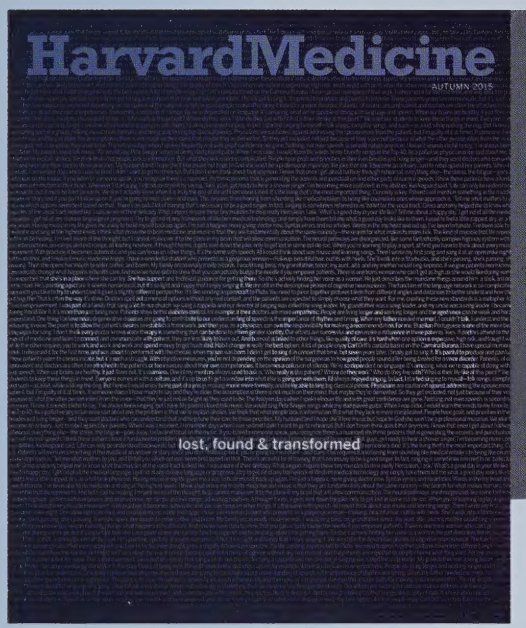
JOHN SOARES

Letters to the Editor

CHART NOTES FROM OUR READERS



After having major surgery, I was dismayed to find that I had lost the bottom and top of my vocal range. Voice therapy brought it back.

THOMAS G. GUTHEIL '67
BOSTON, MASSACHUSETTS

A Mission Continues

I noted with interest the speech therapy advertisement by Sarah Fuller shown in the BackStory section of the Autumn 2015 issue of *Harvard Medicine*.

On October 30, 2015, the Department of Otolaryngology and Communication Enhancement at Boston Children's Hospital celebrated the establishment of the Sarah Fuller Chair for Hearing Loss and Hearing Restoration, which is supported by the Sarah Fuller Foundation for Little Deaf Children. Dora Gay, herself an instructor of deaf children, established the foundation in honor of Fuller, who had been Gay's speech therapy instructor. Fuller served as the principal of Boston's Horace Mann School for the Deaf for more than four decades. One of her pupils was Helen Keller.

When the Horace Mann School closed in 1925, its endowment was used to establish the Sarah Fuller Foundation for Little Deaf Children. In 1957, Gay integrated this foundation into the Hearing and Speech Clinic at what was then Children's Medical Center, Boston. Today, the hospital's Department of Otolaryngology and Communication Enhancement carries on the foundation's mission of comprehensive evaluative and therapeutic services for deaf and hard-of-hearing children.

I was thrilled to see Sarah Fuller's advocation for children with speech impairments highlighted in this magazine.

MICHAEL J. CUNNINGHAM
OTOLARYNGOLOGIST-IN-CHIEF
BOSTON CHILDREN'S HOSPITAL
BOSTON, MASSACHUSETTS

Pipe Fittings

The Voices issue of *Harvard Medicine*, Autumn 2015, struck a chord (!) with me on several levels. I have been a baritone since childhood; my voice never underwent a change, not even at the usual developmental stage. I have spent a half century deeply engaged in choral singing as a second bass, with a range from A two octaves below middle C to F above.

After having major surgery, I was dismayed to find that I had lost the bottom and top of my vocal range. Voice therapy brought most of it back, and, with time and voice lessons, I recovered my original range. Discussing the matter with our chorus conductor, I learned that I should have told the anesthesiologist that I was a singer and that a child's endotracheal tube, rather than an adult's, should be used. This, I was told, might have avoided the post-operative problem. I pass this tip on to readers. Thank you for a great and wide-ranging issue.

THOMAS G. GUTHEIL '67
BOSTON, MASSACHUSETTS

Fine, but Could be Better

I enjoyed, and appreciated, Susan Karcz's article, "How Are You?" which appeared in the Autumn 2015 issue of *Harvard Medicine*; I commend it to those who may not have read it yet.

The article points out that the tone of voice, cadence, body language, and content of both patient and clinician communication are crucial elements of diagnosis and treatment, and that there is a need to "blend" traditional evidence-based medicine and patient-centered care. I would like to re-emphasize everything that was said about work in this domain by those quoted: Dawn Dewitt '90, Elizabeth Gaufberg, and Fidencio Saldaña '01.

Since 2010, my colleagues and I have been involved in evaluating how nurse health coaches, medical students, and residents are trained and in revamping the strategies and techniques used in these trainings. Our project, and subsequent book, *Relationship Power in Health Care*, integrates three theories in psychology that account for the inner subpersonalities of both patient and clinician and presents a new way to train future physicians and nurses so that they can find a place between protecting themselves from being overwhelmed and being able to listen, feel, and genuinely empathize with their patients.

We hope our project will enhance medical education and will stimulate comparative educational trials and additional comparative efficacy research to carry forward our work and that of those quoted in Karcz's article.

JOHN LIVINGSTONE '58
PROVINCETOWN, MASSACHUSETTS

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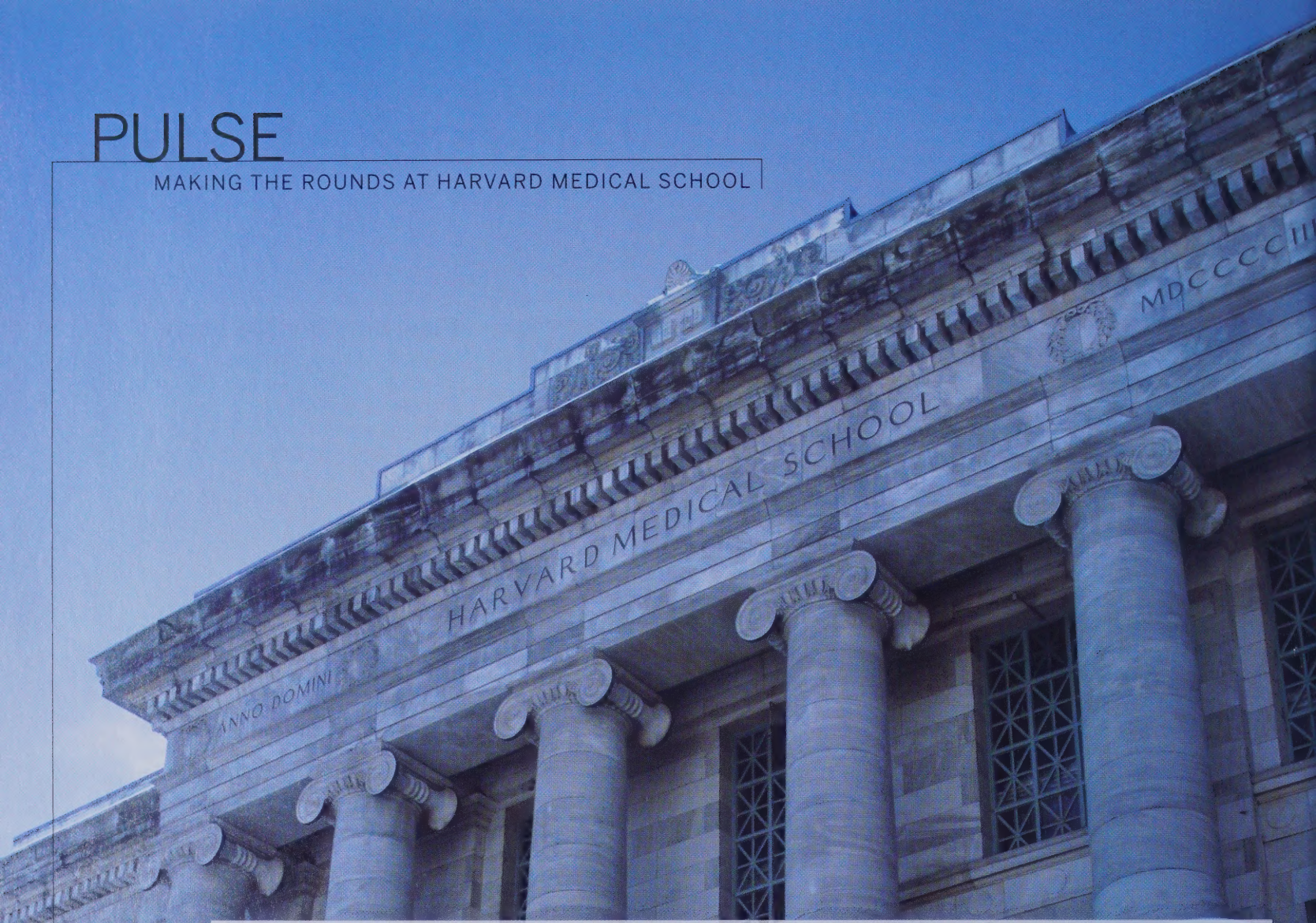


"AN HONOR AND A PRIVILEGE"

HMS dean announces his decision to step down as the School's leader

IN NOVEMBER, JEFFREY S. FLIER, dean of the faculty of medicine at Harvard University, announced he would be stepping down from his post. He shared his reasons in a letter to the HMS community.

"As I approach the midpoint of my ninth year as dean of the faculty of medicine and my thirty-eighth year as a member of this remarkable faculty, I have decided that this is an appropriate juncture to consider transition from my role as dean of HMS.

"Last week, I met with President Faust, who offered me the privilege of serving in this role, and informed her that I plan to leave this office effective July 31, 2016. She has accepted my decision.

"After I step down, I will take a sabbatical year. At its conclusion, I intend to resume my position on the faculty of medicine with a renewed set of personal and professional goals in research, education, and policy.

"It has been an extraordinary honor and privilege—more than words can possibly convey—to have been given the opportunity to serve as your dean and to have been a colleague to so many remarkable people in our extended HMS community.

"I have strived every day over these past eight years to sustain and enhance the sacred mission of the world's leading medical school—set within the world's greatest university—which is closely associated with the finest teaching hospitals and research institutions anywhere. Together we have accomplished so much over these past eight years to strengthen our core missions of education, research, and service. Working together, this large, complex, and remarkable community has made great strides, as the HMS mission statement promises, toward alleviating suffering caused by disease.

"I look forward to working with you during my remaining months as dean, and to then joining you once again as a faculty member and colleague. I hope you know how greatly I have valued your friendship, your partnership, and your extraordinary contributions over these past years."

—Jeffrey S. Flier

A Fork in the Pathway

Final Second Year Show sends up new curriculum

THIS YEAR MARKED the last time that Harvard Medical School's long-running Second Year Show will be produced by second-year HMS and Harvard School of Dental Medicine students. Because of changes in the HMS/HSDM medical education curriculum that took effect this academic year, the show will henceforth be a production of fourth-year HMS students. This year's performance marked the 109th presentation of the show.

"Everyone involved wanted to make it the best show ever because it was the last one," says co-director Laurel Fuentes HSDM '18.

The students did not disappoint. The three-and-a-half-hour show, titled "Brave New Pathways," featured twelve musical numbers based on pop songs and Broadway hits, numerous choreographed dances, a spoof recruitment video, a live pit orchestra, and a cast of more than fifty members of the Class of 2018.

"One of the more fun aspects of being part of this production has been seeing people who have not played instruments or sung in a very long time, if ever, pull talents out of their past or discover undeveloped talents," says the show's music director, Ray Parrish '18. "Even though it's not professional Broadway quality, people are passionate."

Although it poked gentle fun at HMS, "Brave New Pathways" also provided food for thought for those currently navigating the transition to the new curriculum in real life.

"I hope people come away thinking change is the only constant but it doesn't necessarily have to be scary," says co-director Rob Smalley '18.

"I think this show points out a lot of pitfalls that won't come true, but does it in a thoughtful, rather than a cynical, way," adds Parrish. "It makes good lighthearted points about things to keep in mind as all of these transitions are taking place.

"This is a new era of uncertainty; continuously checking oneself and what the School is doing is a good plan moving forward," he adds. —*Stephanie Dutchen*

Together and Apart

Flexible design reflects new curriculum goals

NEW WAYS OF LEARNING require new kinds of classrooms.

The first year of Harvard Medical School's Pathways MD curriculum, which launched this past fall, relies on flexible, case-based, collaborative learning.

Students come to class prepared, having learned basic concepts ahead of time through online readings and brief introductory videos. Class time is spent with faculty solving problems based on the learned concepts.

Students work in small groups of four to six, then form larger groups of around forty to discuss their groups' solutions to the problems posed.

This collaborative approach would have been physically impractical in the existing classrooms in the Tosteson Medical Education Center (TMEC).

"Pathways is a complete rethinking of the MD curriculum for students in the Cannon, Castle, Holmes, and Peabody Societies," says Jane Neill, HMS associate dean for medical education planning and administration. "To accommodate a new kind of learning, we needed a new kind of space." Neill, together with John Scully, HMS associate director of administration for engineering and construction, led the design and construction process for four new three-room learning suites in TMEC.

The new classrooms take advantage of light drawn deep into the building through large exterior windows and glass interior walls. The rooms are further brightened by maple accents and white walls that, in some areas, double as erasable whiteboard space.

The learning studios and classrooms feature movable wheeled tables that can be arranged in a variety of configurations. Each base unit seats two, but for teamwork the tables can be clustered to seat four or more; the whole classroom can also be reconfigured into more traditional arrangements to accommodate conference-room style conversations. Students can even create individual workstations by positioning privacy walls.

The new suites also feature technology that allows teachers and students to share digital resources with one another or, through a simple interface, include other classes and guests at remote locations.

—*Jake Miller*

ONE-A-DAY: Information booklet for a Norlestrin Petipac, circa 1975, from the collection of John Rock, Class of 1918.

JOHN SOARES; THE WARREN ANATOMICAL MUSEUM IN THE COUNTWAY LIBRARY OF MEDICINE (OBJECT)

NOT-SO-BITTER PILL

Oral contraceptive use not linked with increased birth defects risk

ORAL CONTRACEPTIVES taken just before or during pregnancy do not increase the risk of birth defects, according to a study by researchers from HMS, Harvard T.H. Chan School of Public Health, and the Statens Serum Institut in Denmark. The study was published January 6, 2016, in *BMJ*.

The researchers found that for the pregnant women in the study the prevalence of major birth defects was consistent—about 25 per 1,000 live births—regardless of contraceptive use.

"Women who become pregnant either soon after stopping oral contraceptives or while taking them should know that this exposure is unlikely to cause their fetus to develop a birth defect," says Brittany Charlton, an HMS instructor in pediatrics at Boston Children's Hospital and a researcher in the Harvard Chan School Department of Epidemiology.

When used diligently oral contraceptives are more than 99 percent effective: Nearly 10 percent of women, however, become pregnant within their first year of use. Many other women stop using oral contraceptives when planning a pregnancy and conceive within a few months.

While previous studies of the potential health risks to children exposed in utero to the hormones have relied primarily on women recalling their past oral contraceptive use, Charlton and colleagues were given access to a wealth of data collected from multiple Danish health registries between 1997 and 2011. These data were linked to individuals by the unique personal identification number that each Denmark resident is assigned. The researchers looked at data on more than 880,000 live-born infants and their health one year later. Oral contraceptive use by the mother was estimated based on the date of her most recently filled prescription.

Among the women in the study population, 69 percent had stopped using oral contraceptives more than three months before becoming pregnant, while 8 percent had discontinued use within three months of becoming pregnant. One percent, more than 10,000 women, had used oral contraceptives after becoming pregnant.

The prevalence of birth defects was consistent across each category of oral contraceptive use and remained so when the researchers added in pregnancies that ended as stillbirths or as induced abortions.

—Amy Roeder

ISTOCK

Fiber Optics

Neural signs of dyslexia may be present from birth

SOME 5 TO 17 PERCENT OF ALL CHILDREN have developmental dyslexia, or unexplained reading difficulty. When a parent has dyslexia, those odds jump to 50 percent. Dyslexia usually isn't diagnosed, however, until the end of second grade or as late as third grade.

Getting an earlier diagnosis of this disorder may be possible, according to a study reported online on December 7, 2015, in the journal *Cerebral Cortex*, by a research team led by Nadine Gaab, an HMS associate professor of pediatrics in the Laboratories of Cognitive Neuroscience at Boston Children's Hospital. The study indicates that developmental dyslexia can be seen in the brain as early as infancy.

In 2012, members of Gaab's lab found that brain imaging of pre-readers whose average age was 5½ years and who were members of families with a history of dyslexia showed differences in the left hemisphere of the children's brains.

Some researchers proposed that the difference reflects being raised by a dyslexic parent—perhaps, for example, being read to less—but Gaab and colleagues wondered whether the difference could be innate.

To test this question, Gaab's team performed advanced MRI brain imaging on fourteen infants with a family history of dyslexia and on eighteen infants of similar age with no such family history. The MRI scan included a technique that measures the flow of water molecules along the brain's fiber tracts, which indicates how well information flows in the brain.

The scans found alterations in the arcuate fasciculus, a fiber bundle that connects the posterior cortex, which is involved in mapping sounds and word/letter recognition, with the frontal cortex, which integrates and interprets this information.

People who have suffered damage to the arcuate fasciculus often have problems with expressive and receptive language and their ability to manipulate the sounds of a language, a critical part of learning to read. In infants with familial dyslexia, inherited genes may interfere with the prenatal development of the arcuate fasciculus, says Gaab, impairing its structural integrity.

But biology isn't necessarily destiny. According to Gaab, research shows that with early interventions 50 to 90 percent of children with dyslexia can become good readers and that such interventions may lead to normalization of white matter pathways in the brain's left hemisphere.

—Nancy Fliesler

Election Results

Heads of government win greater risk of early death

WE SEE IT HAPPEN ALL TOO OFTEN: The youthful candidate becomes, in a few short years, the grizzled head of state. But is this transformation evidence of normal aging or a health impact of being an elected head of state?

A team of researchers led by Anupam Jena, an HMS associate professor of health care policy, set out to test the theory that politicians elected to lead a country's government may experience premature death. The team's study was published December 14, 2015, in *BMJ*.

After adjusting for life expectancy at time of last election, the team found that elected leaders lived 2.7 fewer years and experienced a 23 percent greater risk of death compared to runners-up.

"This suggests that the stress of governing may substantially accelerate mortality for our elected leaders," says Jena, who is also a physician at Massachusetts General Hospital.

"By comparing the life spans of elected leaders with runners-up, we were able to calculate the mortality cost of winning elections and serving as head of state," says co-author Andrew Olenski, an HMS research assistant in health care policy.

The researchers compared 279 nationally elected leaders from 17 countries to 261 runners-up who had never served in office. The study group was made up of candidates in elections that took place from 1722 to 2015.

The researchers determined the number of years each candidate lived after the last election they ran in and compared the results to the average life span of an individual of the same age and sex during the year of the election.

The researchers say that earlier research by others found no significant effect on the life expectancies of U.S. presidents, perhaps because the sample size was too small. In addition, presidents would be expected to live longer than the general population owing to their higher socioeconomic status alone. The failure of prior studies to detect a difference suggests that the mortality costs of serving as president may have been masked.

—Jake Miller

WIGGLE ROOM

Aging follows no single mechanism

AGING IS ONE of the more mysterious processes in biology. We don't know, scientifically speaking, what exactly it is. We do know for sure when it ends. But what precipitates that endpoint is inscrutable, determined by factors that can often seem statistically random.

Researchers in the lab of Walter Fontana, an HMS professor of systems biology, have found patterns in this randomness, ones that provide clues to the biological basis of aging.

The research team, led by Novartis Fellow Nicholas Stroustrup, found a surprising statistical regularity in how a variety of genetic and environmental factors affect the life span of the *Caenorhabditis elegans* worm. Their findings suggest that aging does not have a single discrete molecular cause but is rather a systemic process involving many components within a complex biological network. Perturb any node in the system, and you affect the whole thing.

The study, in the January 27, 2016, issue of *Nature*, offers an alternative to research that seeks to identify a specific master aging mechanism, such as protein homeostasis or DNA damage.

"There are many important molecular changes that occur with age, but it might not make sense to call all of them 'causes of aging,' per se," says Stroustrup, the paper's first author.

In order to study life span dynamics at the population level, Stroustrup constructed what his team calls a lifespan machine, a device comprising 50 off-the-shelf flatbed scanners. Each scanner was retooled to record 16 petri dishes every hour, totaling 800 dishes and 30,000 worms. The scanners capture images at 3,200 dots per inch, a resolution high enough to detect movements of eight micrometers, or about 12 percent of the width of an average *C. elegans*.

Stroustrup exposed the worms to interventions as diverse as temperature change, oxidative stress, change in diet, and genetic manipulation. The lifespan machine recorded how long it took the worms to die under each condition. Stroustrup then aggregated the data, generated life span distribution curves for each intervention and compared results.

The life span distributions provided considerably more information than just changes in average life span. The research team measured variations arising in ostensibly identical individuals, looking at how many worms died young versus how many made it to old age under each condition. This comprehensive view was important for capturing the dynamics and randomness in the aging process.

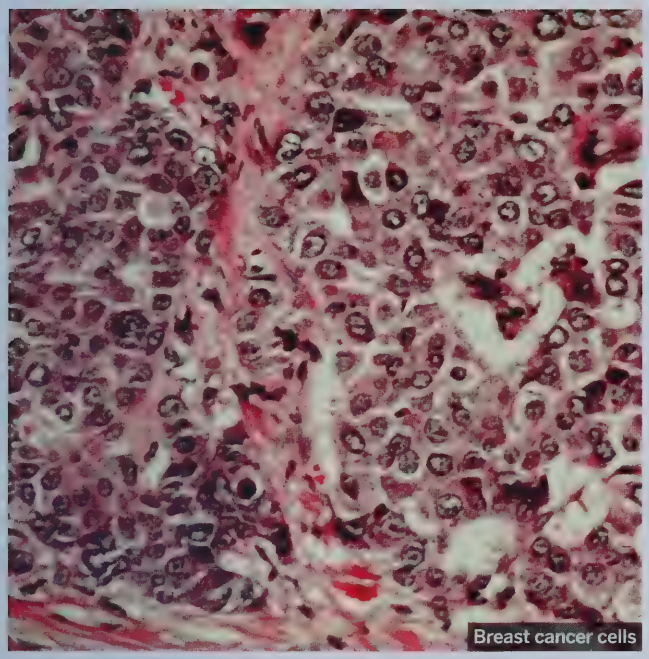
The researchers found an unexpected uniformity among the distribution curves. When all the bell curves were expanded or contracted along the X-axes (which in this study represented time), they became statistically indistinguishable.

The interventions seemed to affect life span in the same way across all individuals in the same population; no matter which genetic process or environmental factor the researchers targeted, all molecular causes of death seemed to be affected at once and to the same extent.

"Life span is a whole-organism property," says Fontana, "and it is profoundly difficult to study it molecularly in real time. But by discovering this kind of statistical regularity about the endpoint of aging, we have learned something about the aging process that determines that endpoint."

Most important, says Fontana, this regularity suggests a profound interdependence in the physiology of an organism so that changes in one physiological aspect affect all others to determine life span.

—David Cameron



Breast cancer cells

Counterpunch

A potential drug and a resistance mechanism found for triple-negative breast cancer

ANTICIPATING CANCER'S ability to reappear after some therapies, HMS scientists at Dana-Farber Cancer Institute have shown the promise of a new drug for a particularly aggressive form of breast cancer and also uncovered a mechanism by which the cancer can outmaneuver the drug. The study was conducted in an animal model and in cell cultures; the researchers plan to move to clinical trials in humans.

The findings, reported in the January 21, 2016, issue of *Nature*, may inform strategies for the treatment of breast cancers classified as "triple-negative," strategies that use drug combinations to simultaneously arrest the disease and prevent it from becoming resistant to front-line therapies. The dual approach could significantly extend patient survival time, the authors say.

Triple-negative breast cancer, so-called because the cancer cells are without three key receptors, is estimated to account for 10 to 20 percent of breast cancer cases. It's often aggressive and tends to have a poorer prognosis than breast cancers fueled by estrogen, particularly in the first five years after diagnosis.

"We found that a class of agents known as BET bromodomain inhibitors significantly impeded the growth of triple-negative breast cancer cells in laboratory as well as animal-model tests," says Kornelia Polyak, an HMS professor of medicine at Dana-Farber. "On the basis of these results, such inhibitors will be tested in patients with triple-negative breast cancer."

"Even if these drugs prove successful," Polyak adds, "we know that cancer often devises a way to circumvent therapies and resume its growth. By understanding the series of steps that allows these cells to become resistant to BET inhibitors, we can now devise approaches that use combinations of therapies to slow or prevent resistance."

A Good Vibe

Stochastic resonance found to alleviate apnea in preterm infants

A VIBRATION-BASED therapy known as stochastic resonance stimulation can successfully treat preterm infants experiencing apnea of prematurity, characterized by disrupted breathing, slowed heart rate, and diminished oxygen levels, according to a study by a team of HMS researchers from Beth Israel Deaconess Medical Center's Department of Neonatology, the Wyss Institute for Biologically Inspired Engineering at Harvard University and collaborators at the University of Massachusetts Medical School.

Reported in the December 2015 issue of *Pediatrics*, the results show that infants' apnea events decreased by half when babies were placed on specially developed mattresses that provided a gentle, soothing vibration similar to a light massage for alternating thirty-minute intervals over the course of three to four hours.

"This simple intervention made a huge difference," says Vincent Smith, an HMS assistant professor of pediatrics, associate director of the neonatal intensive care unit at Beth Israel, and the paper's lead author.

The nervous systems of infants born before 37 weeks' gestation are functionally underdeveloped, and many preterm infants experience periods of apnea during which they briefly stop breathing or do not breathe deeply enough. These infants may also have reduced oxygen levels and slowed heart rates. To manage these symptoms, clinicians frequently treat preterm infants with caffeine, respiratory support, or both.

The researchers studied thirty-six preterm infants in Beth Israel's neonatal unit. The infants were not receiving ventilation support and had exhibited slowed heart rate or diminished oxygen levels. The researchers placed the specially designed mattresses in the infants' cribs and provided them with alternating thirty-minute intervals of on/off stimulation over several three- or four-hour study sessions. The research team simultaneously recorded the infants' heart rate, respiratory rate, and oxygen saturation levels. The researchers then randomized the protocol so that each infant served as his or her own control.

"We could see right away that the stochastic resonance stimulation was successful," says Smith. "These results provide us with proof-of-concept that this approach may be a safe, noninvasive supplemental treatment option for preterm infants." —*Bonnie Prescott*

MATTER OF CONCERN

Airborne particulates heighten cardiac risk for those with diabetes

ALTHOUGH IT'S KNOWN that air pollution is a major risk factor for cardiovascular disease and that some people can be more susceptible to its effects than others, it hasn't been clear who, in particular, might be among those who are more susceptible and why.

Research by investigators from HMS and the Harvard T. H. Chan School of Public Health have now brought some clarity. Using data from a nationwide study of nurses to look for factors that made people more vulnerable to the effects of long-term exposure to particulate matter, the researchers found one that stood out: type 2 diabetes.

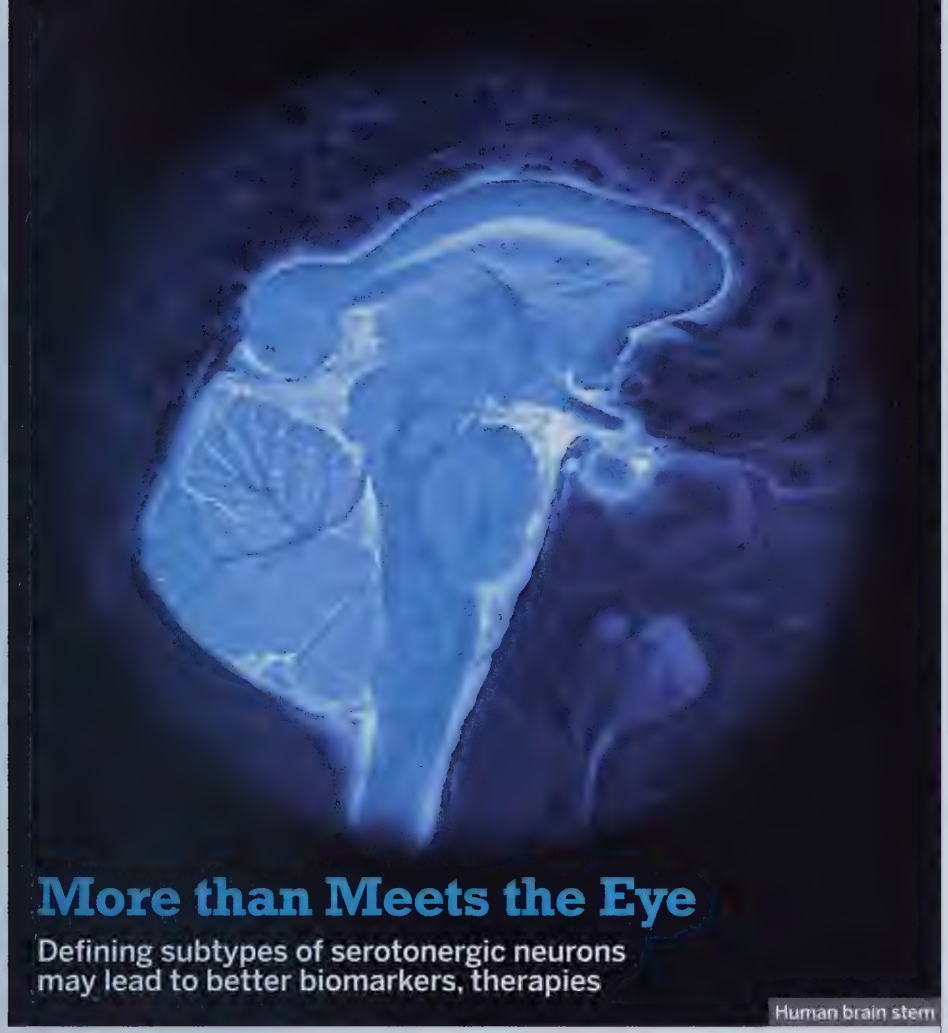
"We didn't expect diabetes to be the strongest factor in determining susceptibility," says study lead author Jaime Hart, an HMS assistant professor of medicine at Brigham and Women's Hospital and an epidemiologist in the Channing Division of Network Medicine at Brigham and Women's and the Department of Environmental Health at the Harvard Chan School. "We looked at age, family history of cardiovascular disease, weight, smoking status, and region of the country, but diabetes was the most consistent across diseases and across different size fractions of particulate matter."

The findings appeared November 25, 2015, in the *Journal of the American Heart Association*.

The research team explored data from more than 100,000 participants in the Nurses' Health Study, looking at rates of cardiovascular disease, specifically, the incidence of coronary heart disease and stroke. They assessed long-term exposure to three different sizes of particulate matter from 1989 to 2006.

Among women with diabetes, increased risk was statistically significant for all cardiovascular outcomes measured and across all sizes of particulate matter. By contrast, among women without diabetes, the researchers found that the increased risk of cardiovascular events as a result of long-term exposure to air pollution was statistically insignificant.

The team found that for each increase of 10 micrograms per cubic meter of air pollution, which is the equivalent of the difference in air quality in a city like Los Angeles, California, and a city like St. Louis, Missouri, a woman's risk of cardiovascular disease increased by 44 percent if she had type 2 diabetes. The team found that these effects were also greater in women who were over the age of 70, obese, living in the U.S. Northeast or South, or had all of these factors.



More than Meets the Eye

Defining subtypes of serotonergic neurons may lead to better biomarkers, therapies

Human brain stem

A RESEARCH TEAM led by Susan Dymecki, an HMS professor of genetics, has reported that serotonergic neurons, which help regulate such processes as mood, appetite, breathing rate, and body temperature, come in at least six major molecular subtypes defined by distinct expression patterns of hundreds of genes. Using a mouse model, the researchers also found that the subtypes vary in their developmental lineage, anatomical distribution, combinations of receptors on the cell surface, and electrical firing properties.

Perhaps of greatest interest, the team showed that a serotonergic neuron's gene expression and function depend not only on its location in the adult brain stem, but also on its cellular ancestor in the developing brain. Their report appears in the November 18, 2015, issue of *Neuron*.

"This work reveals how diverse serotonin neurons are at the molecular level," says Benjamin Okaty, a postdoctoral researcher in the Dymecki lab and co-first author of the paper, "which may help to explain how, collectively, they are able to perform so many distinct functions."

Adds Dymecki, "To have the list of molecular players that make each of these subtypes different from one another gives us an important handle on learning more about what that cell type does and how we can manipulate only that subtype. It holds enormous therapeutic potential."

Although the work was done using an animal model, Dymecki is optimistic that it will be replicated in humans because the serotonergic neuronal system is in a highly conserved region of the brain, meaning that it tends to remain consistent across vertebrate species. Because of this, researchers can look for the same molecular signatures in human tissue and begin to tease apart whether particular subtypes of serotonergic neurons are involved in conditions such as sudden infant death syndrome or autism.

Such research could ultimately reveal previously unknown contributions of the serotonergic neuronal system to disease, inform the development of biomarkers, and lead to more targeted therapies.

The team's findings could also inform stem cell research. "Which subtype of serotonergic neuron are we getting when we use current stem cell protocols?" Dymecki asks. "Can we drive the development of different subtypes? Can we watch how gene expression patterns change over time during development for each subtype?" *—Stephanie Dutchen*

It's the Little Things

Real-time look at microcalcification formation could one day aid cardiovascular patients

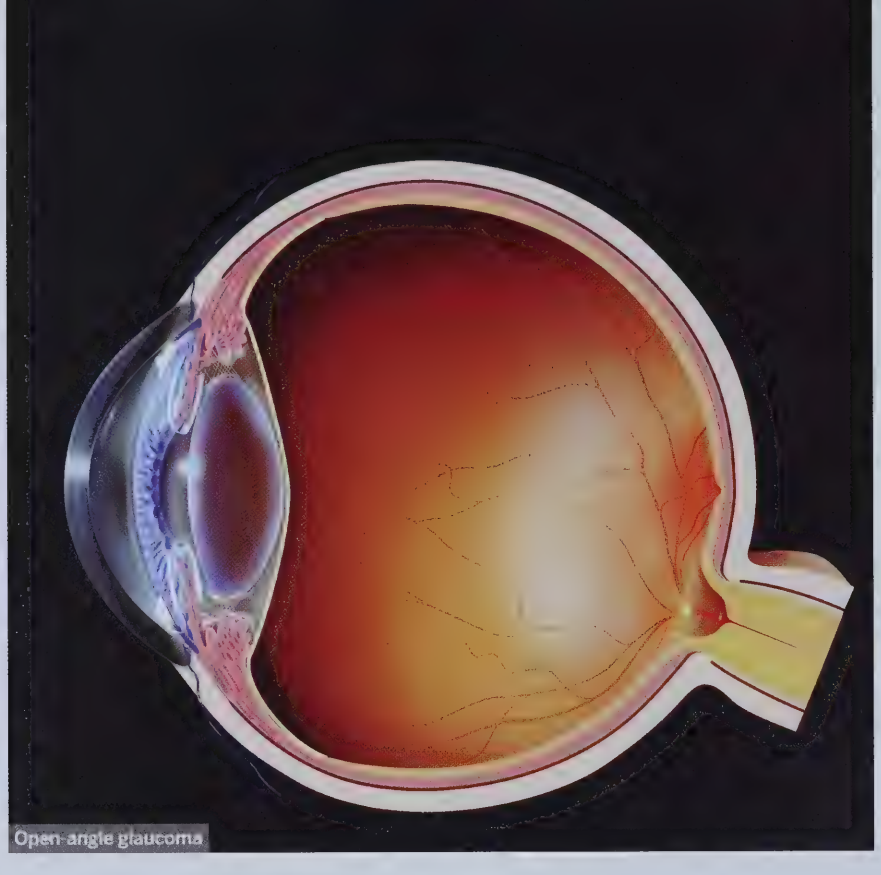
USING RECENTLY developed super-resolution microscopic techniques and a three-dimensional bioengineered model that mimics the connective tissue found in atherosclerotic plaques, researchers from HMS and Brigham and Women's Hospital have followed the formation of cardiovascular microcalcifications in real time, providing key insights into blockages that can lead to heart failure. The team's work could propel innovations in imaging technology that would help advance therapeutic interventions for heart patients. The results of the study were published online on January 11, 2016, in *Nature Materials*.

Coronary calcium scores can predict cardiovascular events in patients, but microcalcifications in the coronary arteries can be so small that traditional imaging techniques cannot detect them.

Using high-resolution imaging techniques, the research team, led by Elena Aikawa, an HMS associate professor of medicine at Brigham and Women's, and Joshua Hutcheson, an HMS research fellow in medicine at the hospital, pinpointed extracellular vesicles that led to the formation of microcalcifications and observed their growth into stable, larger structures or, at vulnerable sites, cause plaque destabilization and rupture—a major cause of heart attacks.

"We can now use this system to visualize what is happening and explore how to intervene in this process," says Aikawa, who also directs the Vascular Biology Program at Brigham and Women's Center for Interdisciplinary Cardiovascular Sciences. "With the knowledge that we've gained here, we can pick out the key extracellular vesicles and find ways to target them before microcalcifications take shape."

The structured illumination and other high-resolution microscopy techniques used in this research cannot currently be used in patients, but the researchers hope that innovations in imaging will help move this technology forward and that future studies of the proteins involved in plaque formation will help identify points of therapeutic intervention. *—Haley Bridger*



Open-angle glaucoma

Vulnerable Points

Three genetic associations identified for primary open-angle glaucoma

AN INTERNATIONAL RESEARCH effort led by scientists from HMS, Massachusetts Eye and Ear, and Case Western Reserve University School of Medicine have identified three genetic associations—*TXNRD2*, *ATXN2* and *FOXC1*—that influence susceptibility to primary open-angle glaucoma, the most common form of adult-onset glaucoma and the leading cause of irreversible blindness in the world. The findings, published online on January 11, 2016, in *Nature Genetics*, provide insights that may ultimately be used to develop gene-based testing and treatment strategies for glaucoma.

"Each genetic association tells an interesting story about the disease," says Janey Wiggs '85, the Paul Austin Chandler Professor of Ophthalmology at HMS, associate director of the Ocular Genomics Institute at Mass. Eye and Ear, and principal investigator on the study.

TXNRD2 produces a mitochondrial protein that regulates the production of reactive oxygen species in cells. When levels of protein are low, these oxygen species can accumulate and kill the mitochondria. The researchers found that reduced levels of the mitochondrial protein is linked with primary open-angle glaucoma.

It was previously known that a nucleotide repeat in *ATXN2* increases the risk of various neurodegenerative diseases, but the scientists also found that gene variants in the repeat regions are linked with primary open-angle glaucoma, suggesting a relationship between neurodegenerative conditions and this form of glaucoma.

Mutations to the protein produced by *FOXC1* are known to cause an early-onset type of glaucoma. The researchers found that genetic variations in a region needed for regulating gene expression is associated with primary open-angle glaucoma, indicating that moderate changes in gene expression influence risk of later-onset disease.

Glaucoma is characterized by a rise in eye pressure that can lead to irreparable damage of the optic nerve, which connects the eye to the brain. In advanced stages of the disease, patients become completely blind. Current treatment for the condition is limited to preventing permanent damage to the optic nerve.

"These studies are beginning to define the molecular events that underlie disease risk, and this is the first step toward gene-based diagnostics and therapies," says Wiggs. —*Suzanne Day*

End Game

Physicians found to forgo intensive end-of-life treatments

RESEARCH BY HMS SCIENTISTS from the Center for Surgery and Public Health at Brigham and Women's Hospital has found that on three of five measures of the intensity of end-of-life care, physicians received significantly fewer intensive interventions than the general population.

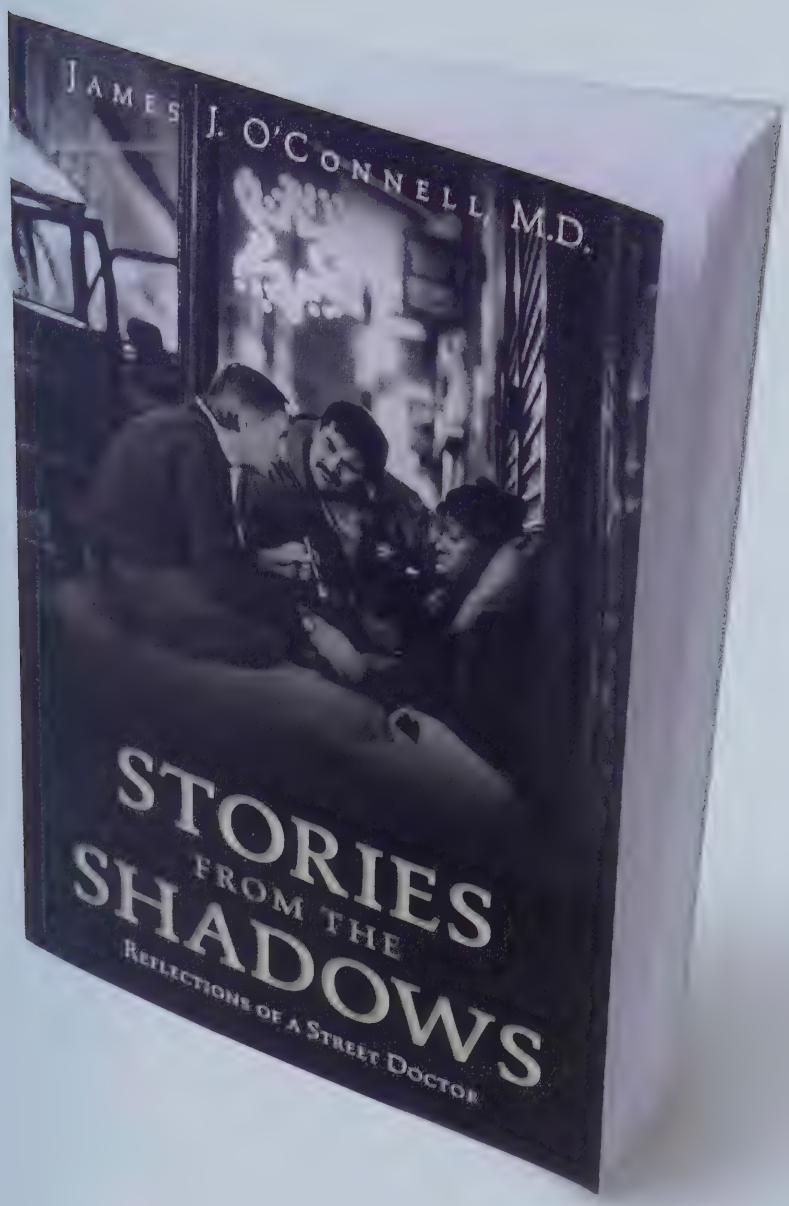
"Our analysis confirms what we've long speculated," says Joel Weissman, an HMS associate professor of health care policy and deputy director and chief scientific officer at the Center, "which is that physicians, who are more likely to have firsthand experience with the burdens and futility of end-of-life care, are less likely to have surgery or be admitted to the ICU during the last six months of life, or to die in the hospital."

Weissman wrote the research letter, which appeared in the January 19, 2016, issue of *JAMA*, with colleagues at the Mayo Clinic and the Center for Research on End of Life Care at Weill Cornell Medical College.

"Patients often ask their doctors what they would do or what they would choose for their own family members," says Zara Cooper, an HMS assistant professor of surgery at Brigham and Women's Hospital and co-author of the letter. "This research could have a significant impact on clinical practice, especially in the way that health care professionals communicate with patients and family members about end-of-life care options."

The analysis included non-health maintenance organization Medicare beneficiaries aged 66 years or older who died between 2004 and 2011 in Massachusetts, Michigan, Utah, or Vermont, and was based on the availability of electronic death records and the ability to link to Medicare data.

The investigators note that additional research is needed to explore how complex decision-making processes and satisfaction with end-of-life care are related to these findings and to see whether the findings will hold true in other states once data become available. —*Emily Wilson*



STREET SIGNS

Stories from the Shadows: Reflections of a Street Doctor by James J. O'Connell
(BHCHP PRESS)

reviewed by Elissa Ely

Stories from the Shadows is slight in length and humbly self-published. It may, as author James J. O'Connell '82 confesses, be "uneven, bumpy, written all too hastily, and dusty from too much time in drawers and boxes." But it recounts formidably the details of homeless lives and insists formidably that these lives be known.

Here are biographical and autobiographical stories from thirty years of street medicine, starting with the first days of the nurse-led clinic at Pine Street Inn, a shelter for Boston's homeless. The medical care is given in shelters, hospitals, respites, and vans that travel the streets at midnight; over conversations about Willa Cather or Aristotle, while tactful physical exams are deftly being conducted; against steady conditions of intoxication and mental illness; and, perhaps most imperatively, during foot soaks.

Some patients are in a constant state of disappearance; others are unable to leave the cardboard house they've built under a loading dock. They care for themselves as they can; one proudly reused a single syringe for insulin over the course of months. They identify themselves (diagnostically) as Tom Collins and Rob Roy. They refuse, accept, then re-refuse, then re-accept care.

Of course, there is no undifferentiated "they" here. The homeless are not a species that can be identified by femur length or tooth. If there's common ground, it's that "the journey toward homelessness is sinuous and treacherous." Medically, as with people in any socioeconomic class, the homeless contract heart disease and cancer, only the courses of their diseases are complicated by resistant infections, by the sequelae of street life (maggot-infested wounds, for one), and by a reluctance to allow workups. One patient refused theophylline levels for her asthma but agreed to re-evaluate the dosage every few weeks, based on the number of detectable wheezes.

They speak in hard-won ways. "When Elise asked me if I've ever heard any voices," says a World War II veteran diagnosed with schizophrenia, "I had to honestly tell her no. I know what she's driving at, and she means mental voices. I told her no, because I hear real voices."

A hundred forms of tender care are described, each with some crystalline detail that embeds it in the mind. The photograph of one patient shows "a wandering right eye [that] glances eerily past the camera into some cosmic distance." This is like a stanza from a late-night poem, written by someone for whom late nights have become a way of life.

And, for the dying, there is a final kind of tender care. When O'Connell describes nurses sitting beside their patient, scenting his pillow with lavender, isn't this what anyone would want?

Does it matter whether my real name is known, or whether it's not?

Elissa Ely '87 is a Massachusetts-based psychiatrist.

Claude Monet
Impression, Sunrise
1872
48 x 63 cm.
Oil on canvas

ALBUM/ART RESOURCE, NY

Eye of the Beholder

Artists tap the circuitry of our visual system to achieve special effects

by Elizabeth Dougherty

Visual art is quite simply made for the human eye. It synchronizes smoothly with how our visual system works, thanks in large part to the astute observations and skills of artists. ■ Over millennia, artists have learned to use color and other tools of their trade to stimulate the brain's visual circuitry in ways that create illusions: depth on a flat surface, movement on a static plane, emotion in an empty space. One does not have to strain to experience these effects. They are simply there, produced by the inner workings of light-sensitive cells in the eye, the complex wiring of the retina, and the trunks and branches of the computational tree that forms the visual cortex.

Piet Mondrian
Broadway Boogie Woogie
1942–43
50 x 50 in.
Oil on canvas

Today, science can explain most, but not all, of how color vision works. Those explanations developed over years of reductionist thinking, meticulous experimentation, and systematic exploration. Yet artists, some working before Sir Isaac Newton revealed that colors were physical and quantifiable parts of what he described as light's spectrum, have managed to feel their way into the visual system, the way a jazz musician might feel his way through an improvisation.

Let the Light In

When light shines on *Launching the Curragh*, a work by the Irish painter Paul Henry, the differently colored pigments in the paint absorb light of differing wavelengths in the visible spectrum. To a large extent, we see what's reflected to our eyes: red light from the men's trousers, yellow from the glistening sand and churning sea foam.

When light from an object or scene enters through the pupil, it is focused on the retina, a wisp of nervous tissue that is actually an extension of the brain. It is this layer of tissue that begins processing visual information in the eye. Its outermost layer is made up of more than a hundred million light-sensitive cells known as photoreceptors. Of these, six to seven million are cone cells that support color vision in humans. These millions of cells are concentrated at the center of the human retina in a region called the fovea.

There are three types of cone cells, each type sensitive to wavelengths of either blue, green, or red light. The tips of these cells are filled with photosensitive pigments known as opsins. When a photon strikes a photosensitive pigment, its chemical structure alters within milliseconds, triggering a cascade of events that results in the transmission of a signal to the brain. Once this series of actions is complete, the chemicals reset, allowing for the seemingly endless translation of light into electrical energy that is perceived by our brain as color.

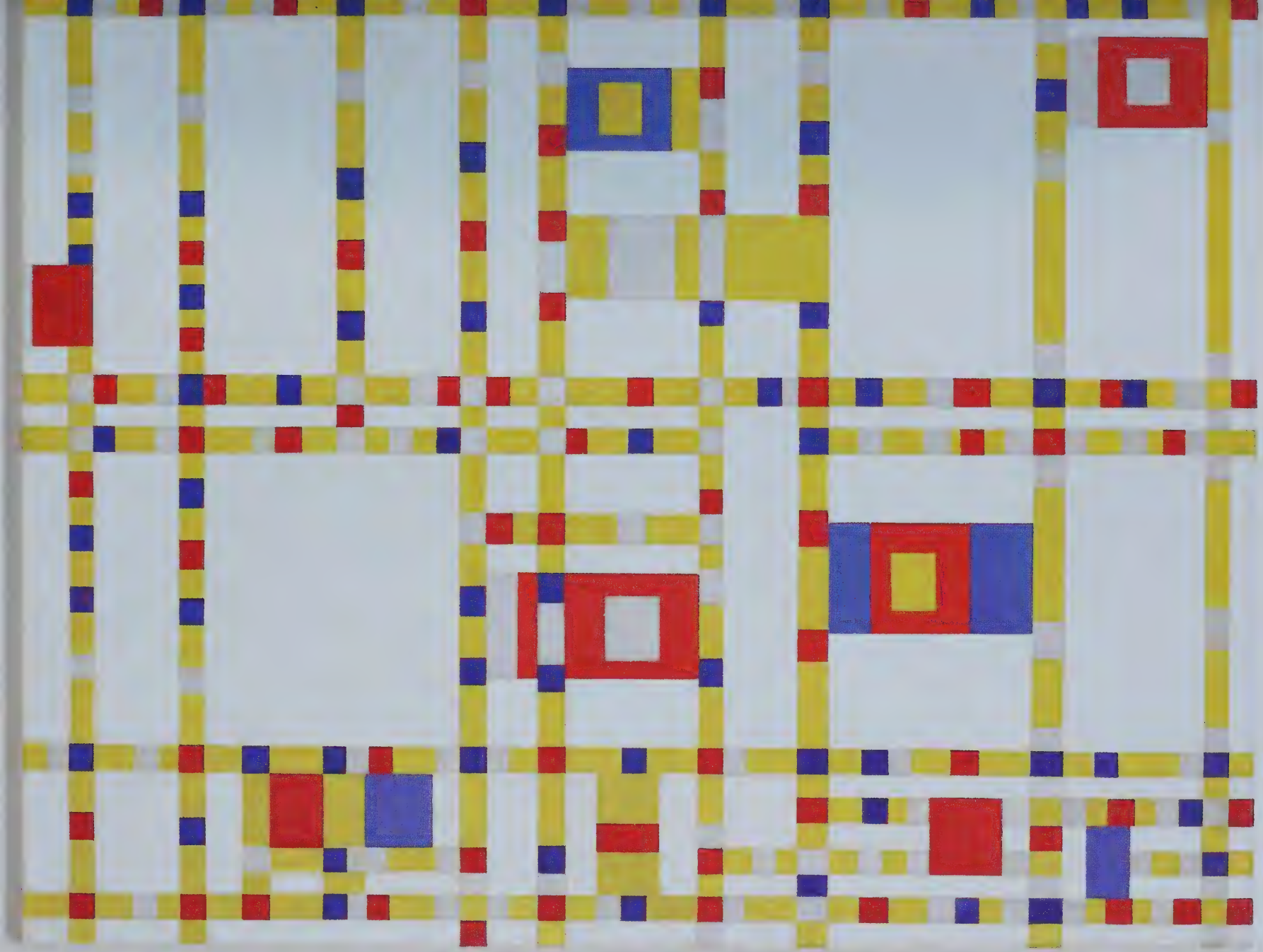
The human visual system is capable of detecting wavelengths between 400 and 700 nanometers, a tiny sliver of the electromagnetic spectrum. Other wavelengths go unseen: the meters-long sound wavelengths that carry voice and song; the tinier-than-the-breadth-of-an-atom wavelengths of cosmic rays that bombard Earth from outer space; and the 100-nanometer wavelengths of ultraviolet light, imperceptible to the eye yet powerful enough to burn the skin.

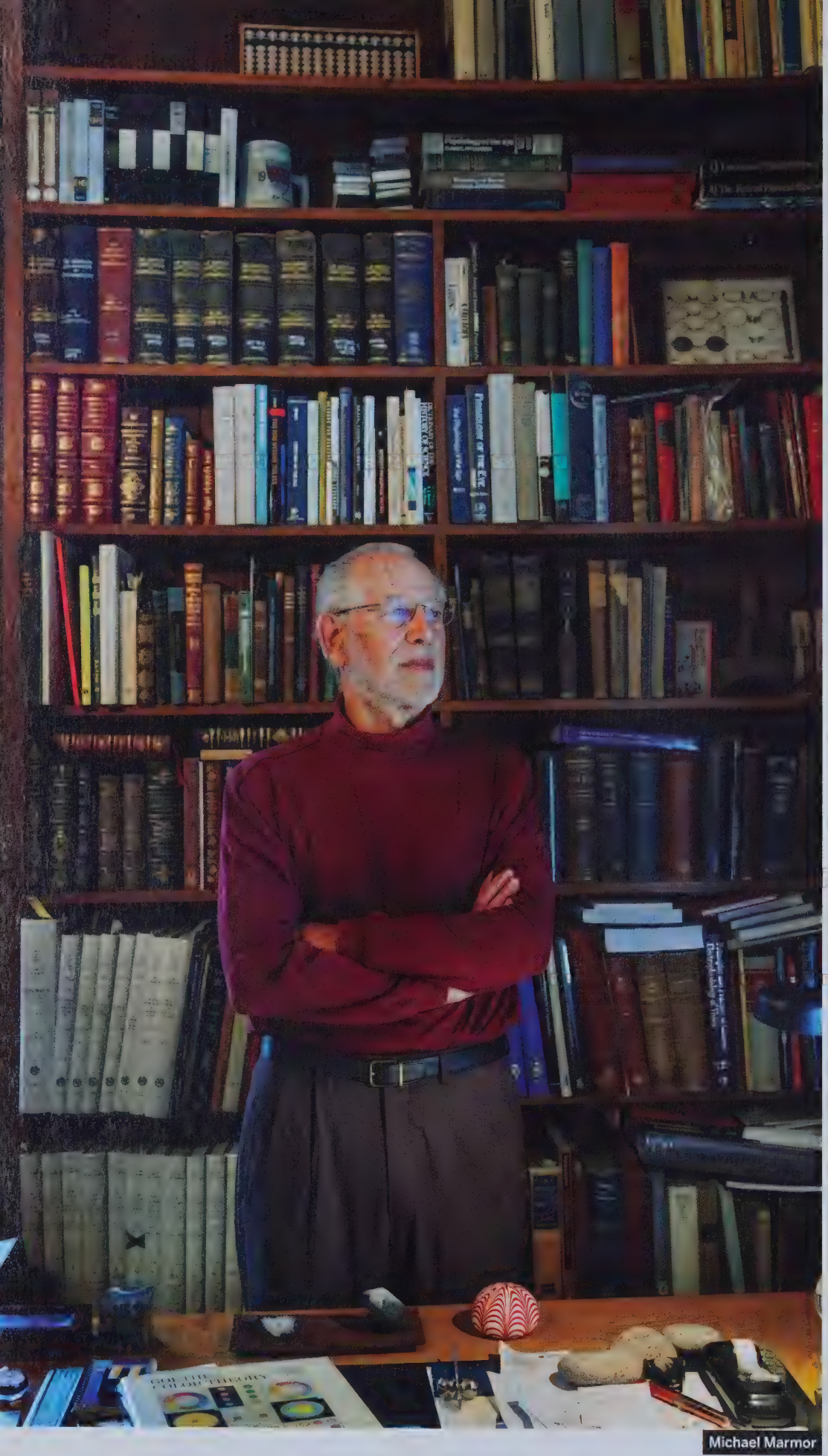
Inky Depths

When John Dowling gives presentations with his wife about vision and art, their focus is on ancient Asian ink drawings. This focus makes sense to each of them: Judith Dowling is an expert in Asian art, and John, the Gordon and Llura Gund Research Professor of Neurosciences at Harvard University, has made it his life's work to study how the retina works and how artwork, such as Asian ink drawings, takes advantage of the visual system's complex wiring to give depth and richness to what is merely black ink on white paper.

The processing that performs this transformation begins inside the eye, inside the retina. The retina is a complex biological computer that, in some species, contains as many as eighty different subtypes of nerve cells and at least ten biologically distinct functional layers that process light signals. The photoreceptor cells that transduce light into electrical signals begin that process.

The photoreceptor cells wire to bipolar and horizontal cells in the outer retina, while the bipolar cells connect to ganglion and amacrine cells in the inner retina. These





Michael Marmor

"We see an object as red not so much because it reflects a discrete wavelength, but because it is more red than the greenness of objects around it."

cells process the incoming signals by making contextual comparisons: How is a spot of light in the center of a field affected by the surrounding light? How is its color affected? Is the spot moving? The layers of wiring create what could be described as parallel streams of specialized movie tracks that represent spots, colors, and motion. The ganglion cells of the retina, which are the output neurons, send these tracks through the optic nerve to cells in the brain's visual cortex for further processing.

"Your eyes are constantly comparing things, so what you see depends not only on what you're looking at but also on the surrounding illumination," says Dowling.

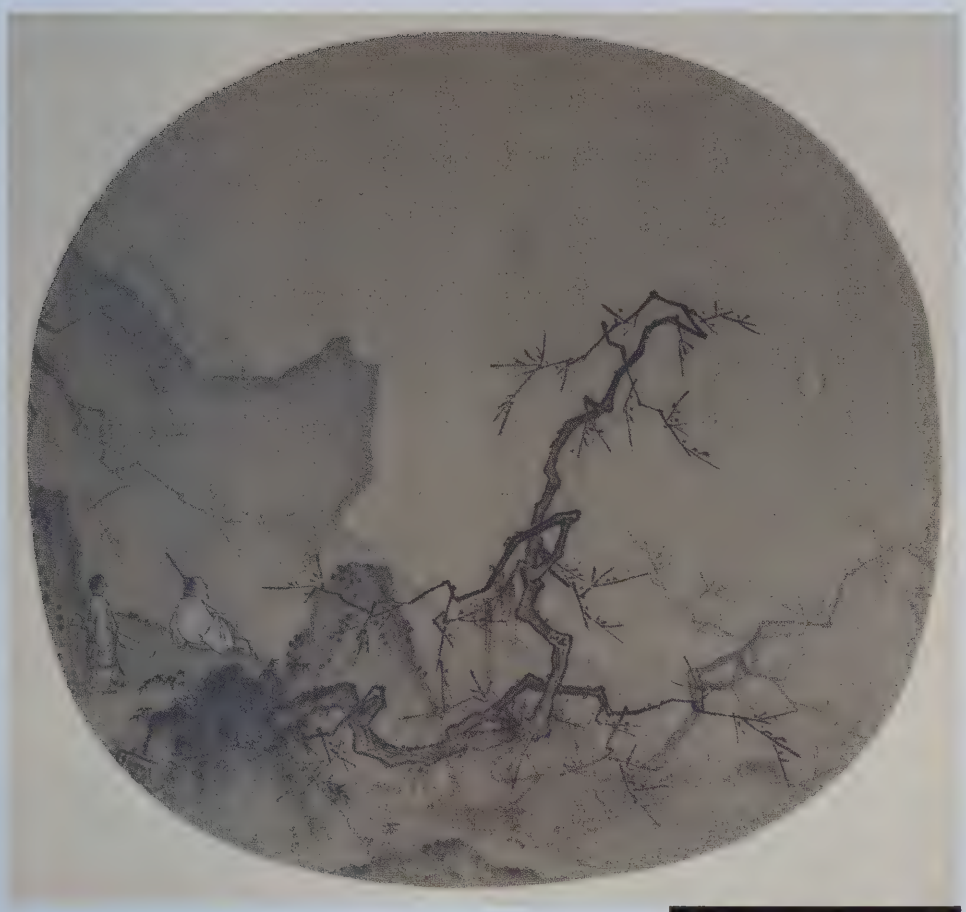
Filling In

Contrast often is at the heart of what makes eighth-century Asian ink drawings so stunning, says Dowling. In *Viewing Plum Blossoms by Moonlight*, a painting by the thirteenth-century Chinese artist Ma Yuan, mountains loom large and forbidding against pale skies even though the heart of the mountain is the same shade of gray as the sky. The eye fills in the mountain's color as it should be, darker than the sky beyond.

"Visual perception is reconstructive and creative," says Dowling. "These illusions work because of what you're expecting to see when you see the outlines in the painting."

The same holds for processing color. The retina goes beyond the detection of blue, green, and red by recognizing local areas of contrast: light and dark, red and green, blue and yellow.

"Contrast is the driver in the retina," says Michael Marmor, '66, a professor of ophthalmology at Stanford University School of Medicine and co-author of the 2009 book *The Artist's Eyes*, which investigates vision and art history. "When we look at a scene,



Ma Yuan
Viewing Plum Blossoms by Moonlight
Southern Song dynasty (1127–1279)
9 7/8 x 12 1/2 in.
Fan mounted as an album leaf; ink and color on silk

we're looking at the complex relationships between forms and colors. We see an object as red not so much because it reflects a discrete wavelength, but because it is more red than the greenness of objects around it."

The retina is so complex that even though Dowling has written two books describing it, neither he nor others have a complete picture of how it works. Recently, he helped launch an effort to use new electron microscopy techniques to construct a precise three-dimensional map of the human retina's central region, which mediates high acuity vision. The work will require him and his colleagues to slice human retinas into thousands of tiny slivers, image them, and then reassemble the images into a complete wiring diagram.

All That Shimmers

Some artists seem to revel in making the visual system, and, by extension the brain, struggle. The French painter Claude Monet was one such artist.

When Monet and others began showing their work in the late 1800s, critics collectively labeled them Impressionists. At the time, the term was meant to be derogatory; now, it is a designation of membership in a pivotal art movement.

According to many, the painting that spurred the critics' ire, and inspired their derisive label, was Monet's *Impression, Sunrise*. In it, a fiery globe hovers over a gray-blue harbor.

And the globe shimmers.

Monet attained this effect through his choice of colors. Color has three components: wavelength, also called hue; saturation, which indicates a color's purity or how free it is of admixture with white; and perceived brightness, which is called value by artists and luminance by scientists.

In *Impression, Sunrise*, it's luminance that matters. Monet brushed in an orange sun that had the same relative brightness as the blue haze surrounding it. The equality of brightness in this painting has been demonstrated using photometry and gray-scale rendering. A gray-scale image, which shows brightness only, effectively erases the sun in the landscape. The sky seems to contain only mottled gray.

According to Margaret Livingstone, Takeda Professor of Neurobiology at HMS, by selecting two colors with the same relative brightness, Monet rattled the brain's visual system. In the 1980s, Livingstone figured out how.

Livingstone and her mentor, the late David Hubel, Nobel Prize recipient and an HMS professor of neurobiology, were trying to map the visual cortex by recording the activity of individual cortical neurons as they applied differing inputs to stimulate an eye.

Around the same time, the lab received a set of slides of tissue from a visual cortex. The slides showed blobs of pale tissue against a dark stained background. To Livingstone and Hubel, the fixed tissue suggested that the visual cortex contained distinct pathways. Their recordings of individual cortical neurons suggested the same thing.

Livingstone used the slides to map her recordings and confirmed that the area of the visual cortex they were investigating contained bands of cells that route signals coming in from the eye to specialized branches of neurons downstream. One branch, dubbed by scientists the "where" pathway, deals with orientation and the location and movement of things in space. Another, the "what" pathway, handles color and shape.

"We have all these modules in our brains for seeing things," Livingstone says. "They make us expert at seeing those things."

Fooling the Experts

Monet's sunrise, however, confuses these expert systems. The where pathway is color-blind: Different hues of the same brightness are identically processed just as black and white photography melds differently colored items of equal brightness. In other words, the where pathway doesn't register the sun in Monet's sky, but the what system finds clear boundaries between the orange sun and the blue sky.

According to Livingstone, when the edges in one pathway don't match up with

Margaret Livingstone

"Artists are really good. They do experiments. They try different things and figure stuff out. They are empirical. Artists are observers."

those in the other, the resulting effect is often some sort of motion—the shimmering of Monet's sun is an example, as are the rotating snakes by Japanese psychologist Akiyoshi Kitaoka and the boogie-woogie cubes in the work of Dutch painter Piet Mondrian.

Over the years, Livingstone has presented her findings about how special and how specialized the visual processing pathways are. Despite her emphasis on the brain and

COLOR THERAPY

What we see is less than meets the eye, especially for those who are color-blind. About ten percent of men are to some degree red-green color-blind. Roughly 1.5 percent of men cannot distinguish reds from greens because they lack either the red- or green-sensitive cone pigments, but for the most part, color blindness results when one of the three types of visual pigments doesn't work normally. A more apt term for this condition might be color deficiency: men who are affected—the condition is sex-linked—see altered or weak colors, rather than no colors at all.

To someone with red-green color deficiency, including the Irish painter Paul Henry, reds and greens are difficult to distinguish. Although Henry used red for the men's trousers in *Launching the Curragh*, he could not differentiate it from yellow or orange. He may well have had help from friends when choosing the tubes of paint to use.

"Artists don't live in a vacuum," says Michael Marmor '66, a professor of ophthalmology at Stanford University School of Medicine. "Friends tell them, 'Grass is green, so use green paint.' There are labels on tubes."

People who are color-blind, however, may one day have an opportunity to experience the full spectrum of color vision, according to Jason Comander '06, an instructor in ophthalmology at Massachusetts Eye and Ear. Researchers at the University of Washington have developed gene therapy that restores the gene that codes for the missing or faulty light-sensitive pigment, allowing cone cells to detect colors that they could not detect previously.

The therapy has been tested in animals that have cone cells sensitive to wavelengths of blue and green light but insensitive to those for red light. A few months after therapy, treated animals could distinguish an image formed from red dots embedded within a field of dots of varying colors, while untreated animals remained blind to the embedded image.

It isn't clear yet whether the therapy works beyond restoring red sensitivity to the cone cells. Does it, for example, also affect the complex wiring inside the retina and the brain that contributes to the processing of color vision within the visual cortex?

Comander finds it amazing that a visual system sensitive to only two colors can gain a third color and that the brain somehow figures out how to recognize the new color. "For any other part of the visual system," he adds, "if you haven't exercised it since childhood, it won't work."

vision in these talks, she's learned that what people remember is the art.

"Artists are really good. They do experiments. They try different things and figure stuff out," says Livingstone. "They are empirical. Artists are observers."

Livingstone has traced one branch of visual processing specialization to the inferior temporal area, a region of the brain that processes faces. Dowling speculates that there is a specialized cortical area that processes color. He bases that speculation on case reports of brain lesions that destroy color vision, but nothing else. These patients see form and movement perfectly well but do not see color.

Ultimately, these branches must reunite so that we can perceive the visual world as a coherent, continuous space, the same ability that allows us to see the sun shimmering in Monet's sky.

"This integration, is called the binding problem," says Dowling. "Right now, no one has a clue as to how it all gets put back together."

Life as Art

Above Livingstone's desk hangs *The Enigma*, a piece of op art by French artist Isia Leviant.

"Someday I'm going to work on that," she says.

So, in the interest of science, I became a test subject.

Standing before the print and scanning the image, I worked hard to find whatever it is that intrigues Livingstone. Photons bombarded my cone cells; the layers in my retina sent signals that revealed edges and purples and oranges to my cortex. Concentric circles and lines took form, but no illusions. I decided to hazard a guess.

"It's moving in and out?"

No, but Livingstone encouraged me. "Surely you see it."

My brain and eyes were working overtime, searching for "it."

More encouragement. "Really? You don't see the nasty motion? The rings have fuzzy stuff spinning in them."

Not to me, they didn't. I sat, defeated. Then, I saw it.

In 2008, neurobiologists in Arizona and Spain figured out that the illusion in Leviant's painting is related to microsaccades, tiny movements of the eye that occur automatically as we gaze at a fixed point, such as the central circle in *The Enigma*. But it's what happens inside the cortex that interests Livingstone.

Even though Livingstone has studied the visual system for decades, she doesn't understand it completely. It's a puzzle. Perhaps the same puzzle as the great binding problem described by Dowling.

Either way, the artist has figured something out. "I wouldn't look at it too long," says Livingstone. She laughs. "It's dreadful."

"I do like it, though," she adds. ■

Elizabeth Dougherty is a science writer based in Massachusetts.

Jason Comander

People with normal three-color vision are trichromats, says Comander, while those with garden-variety color blindness are anomalous trichromats with one pigment being partially defective. Those rare individuals with just two types of cone cells are called dichromats. In contrast, certain females have a four-color visual system; this is a sex-linked trait. Known as tetrachromats, these women have a fourth type of cone cell that is sensitive to a slightly different range of light wavelengths. Tetrachromats may see billions of colors, although among the handful of such women that researchers have studied, only one person was able to distinguish color differences beyond those distinguished by trichromats.

Color blindness can limit career choices. It can, for example, bar individuals from serving as police officers and from engaging in certain roles in the military. Because the condition is so physiologically benign for most affected people, few may be eager to try gene therapy. "There's a cost-benefit to consider," says Marmor.

Testing of a similar gene therapy for achromatopsia, a more serious condition, is slated to begin in 2016, notes Comander. This condition affects cone cells and robs patients of both color and high-acuity vision. It can arise because of missing pigments in the cone cells or because of malfunctions in the cone cells' machinery that transmits light signals to neurons downstream. This novel treatment requires genes that create functioning versions of the faulty machinery to be inserted into cone cells.

"Gene therapy is starting to work and is changing this field," says Comander. "There's a real need for new therapies for the people I see who are losing most or all of their vision due to inherited retinal diseases."

If modern gene therapy does catch on, treatments for color blindness may eventually be approved. That, in turn, could open the door to color vision enhancement.

—Elizabeth Dougherty

A Thousand Words

Stories of medicine unfold on canvas

by Stephanie Dutchen | Images by John Soares

STEADY PROGRESS: Warren and Lucia Prosperi's *Ether Day* painting, which captures the first successful use of ether as an anesthetic, hangs in the domed amphitheater in which the historic event occurred more than 150 years ago.

Alice Flaherty

In Carolus-Duran's *The Convalescent*, a bearded man leans back, exhausted, into a pillow. Carolus-Duran, the name used by nineteenth-century French artist Charles Auguste Émile Durand, brings the viewer into the sickroom, rendering the emotions of illness through light, feature, and posture. ■ Studying this and other such paintings and recognizing elements of her own clinical experience in them has enriched Alice Flaherty's appreciation of sickrooms and deathbeds. It is an appreciation that translates to the clinic.

"I was rounding on a woman who was dying of breast cancer," says Flaherty '90, an HMS associate professor of neurology at Massachusetts General Hospital. "I felt this empathic pain, so I asked her about her suffering. She calmly said she felt at peace, that she had been contemplating the quiet, lovely light in the room."

"I realized that some of my empathy had been the projection of my own distress," Flaherty continues. "Her description of the calm, empty, white spaces of her sickroom gave me the aesthetic distance that allowed me to see more of what was going on with her than I had seen when my eyes were screwed tight with imagined pain."

Whether it's a sickroom tableau, a portrayal of a surgery, or a portrait of a clinician or researcher, depictions of medicine in art have wide-ranging effects on those who view them. In addition to revealing the beauty in everyday clinical care, art inspired by medicine can connect doctors with the history of their profession, encourage them to confront ambiguities or consider alternative points of view, help situate their experiences within a larger context, soothe or sharpen emotions, and lead them to improve patient care in unexpected ways.

Artists, subjects, and viewers connect on another level when the process for reconstructing a historical event in medicine or capturing the character of a portrait subject entails the same meticulous collection of data and keen observational skills practiced in medicine. That physicians and painters should find one another kindred spirits is not surprising given the intertwined histories and philosophies of naturalist art, science, and medicine.

Nature Studies

Ask Massachusetts-based artists Warren and Lucia Prosperi whether they feel an affinity with physicians and scientists, and they will elaborate on how they share a fascination with the nature of the human experience. To capture this fascination in their paintings, they allow themselves to be endlessly curious about the subject, struggle to balance involvement with detachment, and pursue their desire to craft scientifically accurate images based on close observation.

"We're empiricists," says Warren, a painter who, in collaboration with his wife, a photographer, has produced dozens of paintings for HMS-affiliated institutions. Most notable, perhaps, is their *Ether Day*, a work completed in 2001 and displayed in a surgical amphitheater, dubbed the Ether Dome, in the Bulfinch Building at Mass General. In that room in 1846, the use of inhaled ether as a surgical anesthetic was first demonstrated successfully.

The Prosperis adhere to the principles of naturalism, a movement that arose in Europe in the mid-nineteenth century as

ARTISTS-IN-RESIDENCE: Warren and Lucia Prosperi's studio contains several of the historical works on which they have collaborated, including *The First Casualty at Bunker Hill*, shown here, in part.

writers, visual artists, and filmmakers, inspired by advances in natural science, sought to apply scientific methods to their work. Reacting against the idealism and symbolism of romanticism, naturalist painters presented realistic depictions of everyday life with as little distortion as possible. An example of this style, and one that is among the more pervasive images of the caring physician in art, is the late-nineteenth century painting *The Doctor* by British artist Sir Samuel Luke Fildes. In the work, Fildes portrays a pensive clinician keeping watch over an ailing girl while her parents look on helplessly.

Naturalist artists gather vast amounts of data to ensure accuracy, and the Prosperis are no exception. They spend hours talking with and photographing portrait subjects until they're satisfied that they've captured not only minute physical details but also the person's essential character. For posthumous portraits and historical scenes, they conduct exhaustive archival research, consult experts on the period, and interview anyone who might have known the person or experienced an event firsthand.

"They sucked my bone marrow for details," says Donald Barnett, a former HMS assistant clinical professor of medicine and now curator of the Joslin Diabetes Center Historical Commission. Barnett has advised the Prosperis on seven paintings depicting landmarks in Joslin's history.

As a clinician, Barnett appreciates thorough information gathering. "Historical records tell the 'what,' not the 'how,'" he says. "We brought in the details to turn a painting into a story, and we had a fanaticism for telling the story correctly."

Details, Details

Demonstrating the effective use of ether during surgery launched U.S. medicine into the international spotlight. Little wonder that when planning to commemorate the 150th anniversary of that landmark event, the hospital's service chiefs and physicians commissioned the Prosperis to paint a historically accurate version of what happened that day. The research the Prosperis undertook for *Ether Day* illustrates their dedication to telling stories correctly.

Although written documents and photographs yielded plenty of facts, crucial questions remained: Was surgeon John Collins Warren right- or left-handed? What was the nature of the incision he made? To what

extent would red blood cells have oxidized and begun to separate from plasma in the basin used to capture the blood that flowed from the incision? Where would Warren and dentist William T. G. Morton, who administered the ether, have stood relative to the patient?

Over time, a detailed picture took shape. Whenever the Prosperis reached the limits of evidence, they and their consultants made logical deductions. Daguerreotypes in Harvard's Fogg Museum, for example, show Warren holding his glasses in a manner that suggests he was right-handed. If true, that would mean he should be positioned to the patient's right in the painting. The fact that blood would flow from the incision—this was a time before cauterization was used—meant someone would probably be there to sop it up, so given Warren's position, the Prosperis put that person on the patient's left along with a basin on a table. The possibility that ether wouldn't work would have meant that the surgical team not only used restraints at the patient's elbows and ankles but also assigned someone to hold the patient's head still, likely from behind to remain out of Warren's way. Thus, each decision about how to compose the scene helped another fall into place.

Reconstructing events feels like time travel, the Prosperis say, and that sense of witnessing the past with nearly photographic precision gets shared with the viewers.

"I remember being alone in the Ether Dome, feeling the history of that moment, and thinking that we had to do honor to what came before," says Lucia. "It was a heavy responsibility."

Adds Warren, "It was also great fun."

Shades of Meaning

Beyond authenticity, the choices made in paintings of medical topics take on symbolic value and convey what it means to be a doctor, a patient, or part of an institution.

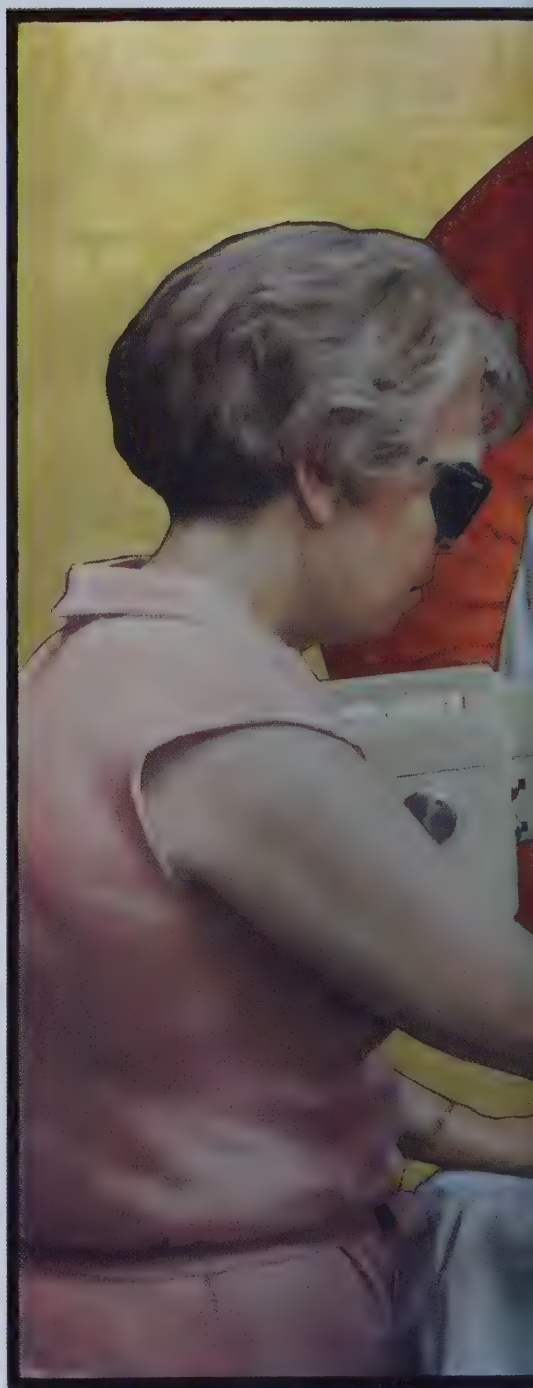
The doctor's worried expression in Fildes' iconic painting reminds practitioners that sometimes medicine reaches its limit and all it can offer is empathy with the human experience. When English artist John Collier turns the physician away from the viewer in his 1908 painting *Sentence of Death*, he is subtly directing the viewer's gaze to the young male patient and his shocked expression, emphasizing how personally devastating the receipt of a terminal diagnosis can be. In *Science and Charity*, executed by the Spanish painter Pablo Picasso when he was 15 years old, the artist presents the doctor as the scientific observer of symptoms, focusing on his timepiece as he takes his patient's pulse while a nurse provides compassionate care.

Beyond authenticity, the choices made in paintings of medical topics take on symbolic value and convey what it means to be a doctor, a patient, or part of an institution.

Paintings can also capture the moment a clinical procedure was first put into practice, such as the 1816 introduction of the stethoscope depicted in Ernest Board's sunlit *Laënnec Listening to the Chest of a Patient*. In Board's 1908 work, the early monaural cylinder itself and inventor René Laënnec take center stage. Although such paintings can boost present-day doctors' and researchers' confidence that their contributions could likewise change the course of medical history, artistic works can also be used to warn that not all new ideas pan out. For better or worse, French physician Simon Bernheim immortalized his hypothesis for curing tuberculosis using interspecies blood transfusions by hiring French naturalist artist Jules Adler to advertise his idea, which Adler did in *The Transfusion of a Goat's Blood*.

When Barnett led the team choosing the subjects for the Joslin paintings, he tried to select caregivers and researchers who represented progress in diabetes research and treatment and to tell stories that embodied the Joslin's values. One of the physicians selected was Priscilla White, a founding member of Joslin Clinic. White, who collected data from pregnant women for half a century, helped raise the survival rate of babies born to diabetic mothers from 56 percent to over 90 percent.

Another painting depicts a twentieth-century health care team conferring around the bed of a woman with diabetes and a



EYE TO INNOVATION: In a mural for the Joslin Diabetes Center, Warren Prosperi depicted HMS faculty William Beetham, a surgeon; Lloyd Aiello, an ophthalmology professor; and Priscilla Holman, a nurse, performing a laser surgery procedure developed by Beetham and Aiello. The revolutionary procedure prevented bleeding-induced blindness in patients with diabetes.

foot infection. Although some people recoil from the "blood and guts" nature of the gangrenous limb, Barnett says, he believes it's important to portray real patients who lose their legs to the disease. "Looking at the painting reminds doctors of the importance of taking care of the whole person," he says.

Viewers' reactions can be emotional as well as intellectual. For Barnett, standing in the Joslin lobby surrounded by the Prosperis' paintings brings back fifty years of memories of caring for patients with juvenile diabetes.

"Tears would come to my eyes to see kids in their twenties going blind," he says. "This art can make people aware of what it was like to be a patient or a doctor in those days, when diabetes was a war."

Face Values

The walls of Flaherty's office are papered with taped-up printouts of artwork by and about doctors and patients. Art books and sculptures crowd all available horizontal surfaces. Flaherty believes that repeated exposure to artistic renderings of bodies and illness can make them less threatening in reality, help health care practitioners process difficult clinical experiences, and reassure practitioners that their work fits into an older, larger context.

Nonetheless, she worries about putting too thick an aesthetic gloss on medicine.

"It makes our patients more interesting and less painful for us when we aestheticize their experience, but that also can over-anesthetize our ability to feel their pain," she says.

Art, cautions Flaherty, can encourage doctors to ignore the messiness in real patients' stories or to infer emotions that may not reflect patients' actual experiences and feelings. It can, she adds, perpetuate an approach of treating patients like objects to be contemplated rather than as active participants in their own care.

At the same time, Flaherty is among those who believe that art serves doctors well when it "takes something that we encounter every day, and thought we knew, and makes us see that it is unique."

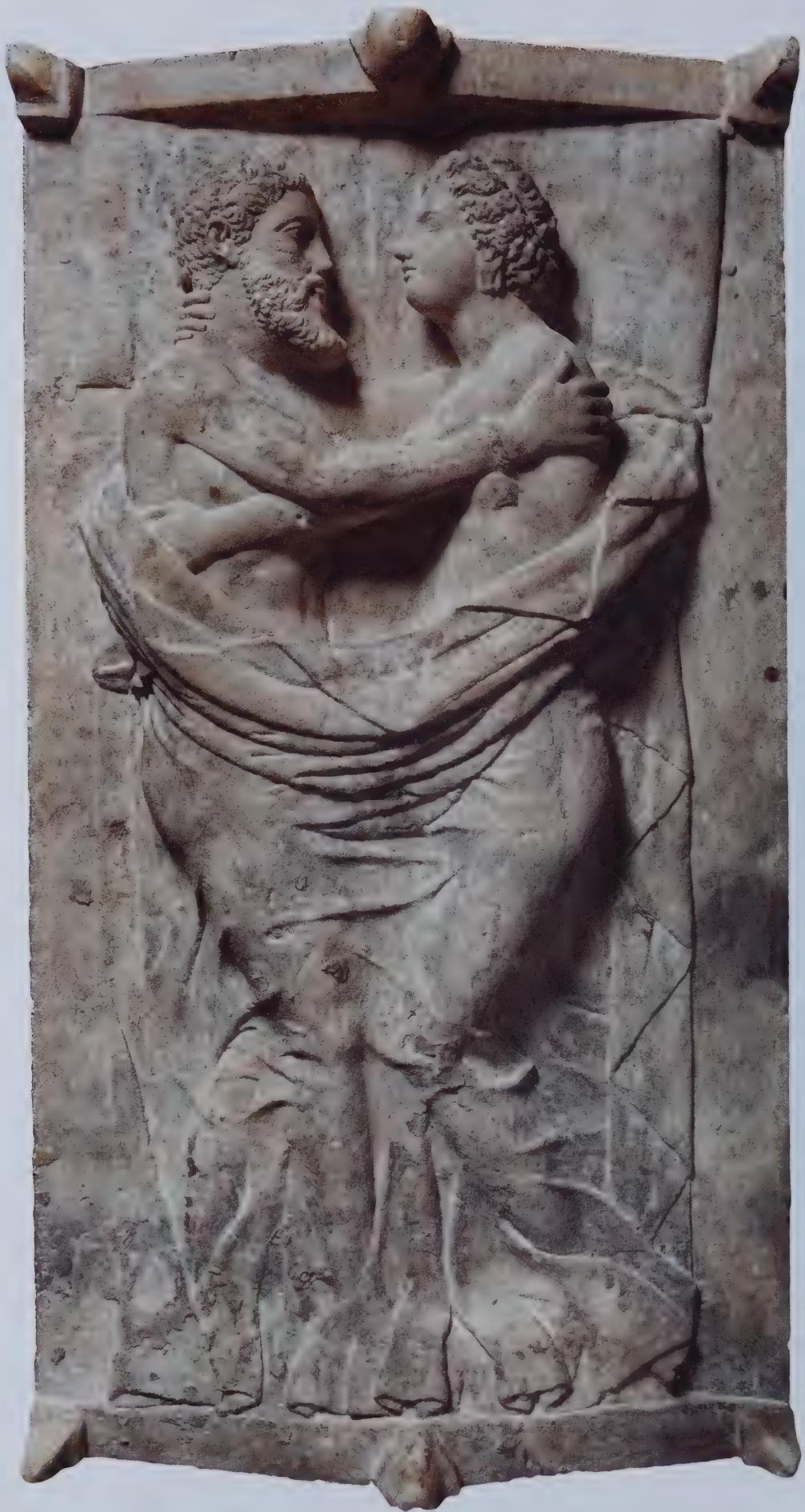
Having witnessed physicians refer to a terrified-looking patient as "resting comfortably," Flaherty thinks that art can teach doctors to pay attention.

"Doctors often see the jaundiced sclera but not the sad expression," she says, "because it saves time if we ignore the pain. Looking closely at portraits can help us remember how to look at people."

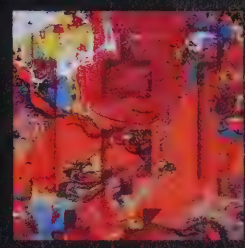
Flaherty says that close attention to facial expression helps her tell the impassivity of depression from that of Parkinson's disease, Botox treatments, or simply personal demeanor. Occasional attempts to draw—Flaherty has taken some lessons from Warren Prosperi—have engaged her with patients' affect even more. She has learned, for instance, that if an eyelid's position changes by even a hundred microns, a face can be transformed from sadness to fear.

"I was talking to a patient once and said, 'Oh, the light's in your face,'" Flaherty remembers. "He said, 'That's so thoughtful of you.' Don't thank me, I thought, thank an artist." ■

Stephanie Dutchen is a science writer in the HMS Office of Communications and External Relations.



Sarcophagus and lid with husband and wife
Italic, Etruscan, Late Classical or Early Hellenistic Period, 350–300 BC
Travertine
36 3/4 x 46 1/4 x 84 3/16 in.
Museum of Fine Arts, Boston



Art unleashes emotions and discussion among new doctors **by Michael Blanding**

MUSEUM STUDIES

On a quiet Thursday night several years ago, Ray Williams was discussing the carvings on an Etruscan sarcophagus, housed in Boston's Museum of Fine Arts, with a group of internal medicine interns from Brigham and Women's Hospital. Carved from travertine some 2,300 years ago, the sarcophagus was large, nearly the size of a hospital bed, with a lid that featured a man and a woman lying frozen in a loving embrace, half covered by stone "sheets."

"They wanted to be buried together, not shown as Greek gods with perfect bodies, but as a middle-aged couple who loved each other," the art educator told the group of freshly minted doctors. "I picked this work because I thought it might call up some images from your work in the hospital."

In the uncomfortable silence that followed, Williams worried he had made a mistake. "Maybe I'm wrong," he started to apologize. "I was trying to pick something relevant to your experience."

"No," said one member of the group, "it's very relevant." Just a few days ago, the resident said, he'd told a husband that his wife of fifty years was going to die of cancer. "I was supposed to know what to say," he continued. "I felt so inadequate." Other members of the group murmured their deep understanding of this experience, indicating that they, too, felt ill-prepared for these early conversations about death and loss.

"Sharing their feelings of inadequacy was a new experience for these young people," says Williams, a former director of education at the Harvard Art Museums and now the director of education and academic affairs for the Blanton Museum of Art at the University of Texas at Austin. Since that night, hundreds of HMS interns and residents have gone through a similar exercise, using art as a catalyst for discussions about the challenges and difficulties they face as physicians.

"Taking them out of the wards and into a museum environment," says Joel Katz, an HMS associate professor of medicine at the School, vice-chair for education in the Department of Medicine at Brigham and Women's, and director of the hospital's internal medicine residency program, "can give them needed space to reflect on their experiences in a deeper, more reflective human way."

Ray Williams

"We are committed as a residency program to training great doctors," he adds. "But we are also committed to creating well cared-for caregivers in order to achieve that goal."

Beholding

Art is increasingly a part of education programs at medical schools throughout the country. Educators use the paintings and sculptures in nearby museums to help students to not only develop empathy and talk about their feelings but also to hone their diagnostic and communication skills and their ability to work in teams.

"A great work of art doesn't just copy reality," says Shahram Khoshbin, an HMS associate professor of neurology at Brigham and Women's, "it also brings emotion into it. Whenever you bring in emotion, that consolidates memory and aids in learning."

At HMS, the effort to use art in medical education began more than fifteen years ago when a group of students approached the dean with research showing that the study of art had aided dermatology students at Yale in diagnosing skin conditions. Katz, who had worked as a graphic illustrator before medical school, was intrigued. He contacted Khoshbin, who had written his college thesis on Vincent Van Gogh and epilepsy and was himself an artist.

"Observation is still ninety percent of what we do," says Khoshbin. "All of our new technologies are not going to change the fact that there is a patient-physician interaction."

No courses at the time, however, specifically taught visual literacy skills. Katz and Khoshbin developed a course based on Visual Thinking Strategies, a method for teaching children co-developed by Harvard-trained psychologist Abigail Housen and former Museum of Modern Art education director Philip Yenawine. At its core, the course consists of asking three simple questions about artwork: "What's going on in this picture?" "What do you see that makes you say that?" and "What more can we find?"

Katz and Khoshbin used those questions to create the ten-week class Training the Eye: Improving the Art of Physical Diagnosis for preclinical medical students at HMS. The course includes visits to museums such as the MFA, the Harvard Art Museums, and the Isabella Stewart Gardner Museum to develop visual skills that are then applied in the classroom and to patient care.

"The skill might be deciphering patterns and texture, and then we return and look at dermatology slides," explains Katz. "Or the skill might be symmetry, and then we review the findings of normal and abnormal cranial nerves."

Class Project

From the course's inception, Katz and Khoshbin empirically tested how effectively it trained students. In a 2008 study published in the *Journal of General Internal Medicine*, Katz, Khoshbin, and their co-researchers described their methodology and findings.

A group of students in the class and a group of control students were shown a set of pictures of artworks and medical conditions before and after the course, then were graded by independent examiners, who were not aware of timing or participation status, on how many accurate observations of medical conditions the students made. When before-course and after-course measures were compared, students who had taken the Training the Eye course improved the frequency of their observations by 38 percent, while the control group showed no such improvement.

"The descriptions of the observations made by members of the test group were far more sophisticated than those of their fellow students," says Khoshbin.

Improvements to visual skills are only part of what art can provide to doctors' training, however. In 2008, Barbara Martin, Alfond Curator of Education at the MFA, asked Katz if there were ways that the museum could work with other medical practitioners; the result was a workshop for residents that focused on reflection, empathy, and self-care

Joel Katz

REGINALD CAMPBELL (OPPOSITE); JOHN SOARES

as well as observation and communication. That overture led to the development of a one-night program in which first-year residents would use art to reflect on their experiences. The program is now part of the Humanistic Curriculum, a required wellness program for internal medicine residents at Brigham and Women's.

The program consists of five exercises, each lasting around 15 minutes, in which museum educators show the residents different pieces of art in the museum and encourage them to talk about what they see. During a recent meeting, the physicians were introduced to a contemporary work by artist Susie Ganch, part of a recent exhibit at the museum. The work consists of an 11-foot string of recycled objects that tapers from a large aggregation of white disposable spoons and coffee cups to a narrow collection of pink and red buttons and pieces of plastic. The students are asked to talk about how the artwork might be a metaphor for their lives.

"One group decided that, as a beginning resident, you have a lot of information in your brain but as you continue you become more focused, centered, and confident," says Brooke DiGiovanni Evans, the MFA's head of gallery learning, who has succeeded Martin as the leader of the program. "Another group had the opposite feeling, that you start with very little knowledge about what you are doing, but as you gain knowledge you realize the greater complexity of the job."

The specific responses are almost beside the point, compared to the opportunity the experience provides young doctors to talk about the difficulties of their residency—discussions and comparisons that the open-ended nature of contemporary art is capable of triggering. "Contemporary art can be a springboard to use as a way to understand something, to understand yourself," says Martin.

"For almost every culture, death is one of the points at which they turn to art."

Physicians who might be reticent to open up in a group discussion at work may be more comfortable sharing their thoughts in the stress-free environment of an art museum. "Doctors mention that the hierarchy that exists in a medical context doesn't exist in a museum," says DiGiovanni Evans. "Everyone is pretty much on the same ground in terms of understanding how to engage with a work of art."

A Level Field

That message is more explicit in a program that Williams developed with Mary Thorndike '02, an HMS instructor in medicine at Brigham and Women's. This effort brings teams made up of doctors, nurses, residents, and physical therapists into the museum to discuss art.

"The interpretive problem a work of art poses is comparable to the diagnostic problem a medical case poses," says Williams. "Rather than looking at art as a solitary experience, they work as a team to solve a complicated interpretive puzzle."

In the hierarchical setting of a hospital, the opinions of some, particularly those with seniority, carry more weight than those of others. In front of a complex piece of art, however, no one's expertise is prized over anyone else's.


Shahram Khoshbin

"When you realize a medical student had the most important insight and that a nurse then added observations that others hadn't made, it helps you recognize the importance of everyone's opinion," says Katz.

Being confronted with a challenging piece of art also offers a lesson in tolerating ambiguity. In programs for medical teams held at the Harvard Art Museums, Williams always liked to end with a mixed-media sculpture by Rachel Harrison. This piece involves a life-size child mannequin wearing multiple masks, staring up at a torso in a gaudy dress, all topped by a grinning skull. Inevitably, says Williams, teams get stuck on trying to figure out what it means.

"That search for the work's meaning becomes a conversation about who you are in the face of uncertainty or ambiguity," he says. "Some people will just bluster through and try to get others to believe them. Others get really quiet and opt out of the conversation." By examining their own tendencies in the relatively low-stakes venue of the art museum, the team members gain insight into how they might react in a high-stakes medical situation.

Some groups surprised Williams with the way they created meaning together, informed rather than hindered by their experiences in the hospital. One team saw Harrison's sculpture as one of a child coming to terms with mortality, the green-wigged skull representing the child's mother. According to Williams, that group then had an entire conversation about what it feels like for this child to be in close proximity to death—and to remain there with integrity. "Something," Williams adds, "that is not so different from what a physician experiences."

Brooke DiGiovanni Evans (left) and Barbara Martin

Noble Truths

The hospital and the art museum, in fact, may not be dissimilar. Both are full of traumatic images that challenge society's taboos concerning physical contact, nudity, blood, sickness, violent injury, and death.

"For almost every culture, death is one of the points at which they turn to art," says Martin. "A lot of the art in this building relates in some way to commemorating the dead or honoring the dead or preparing for the afterlife."

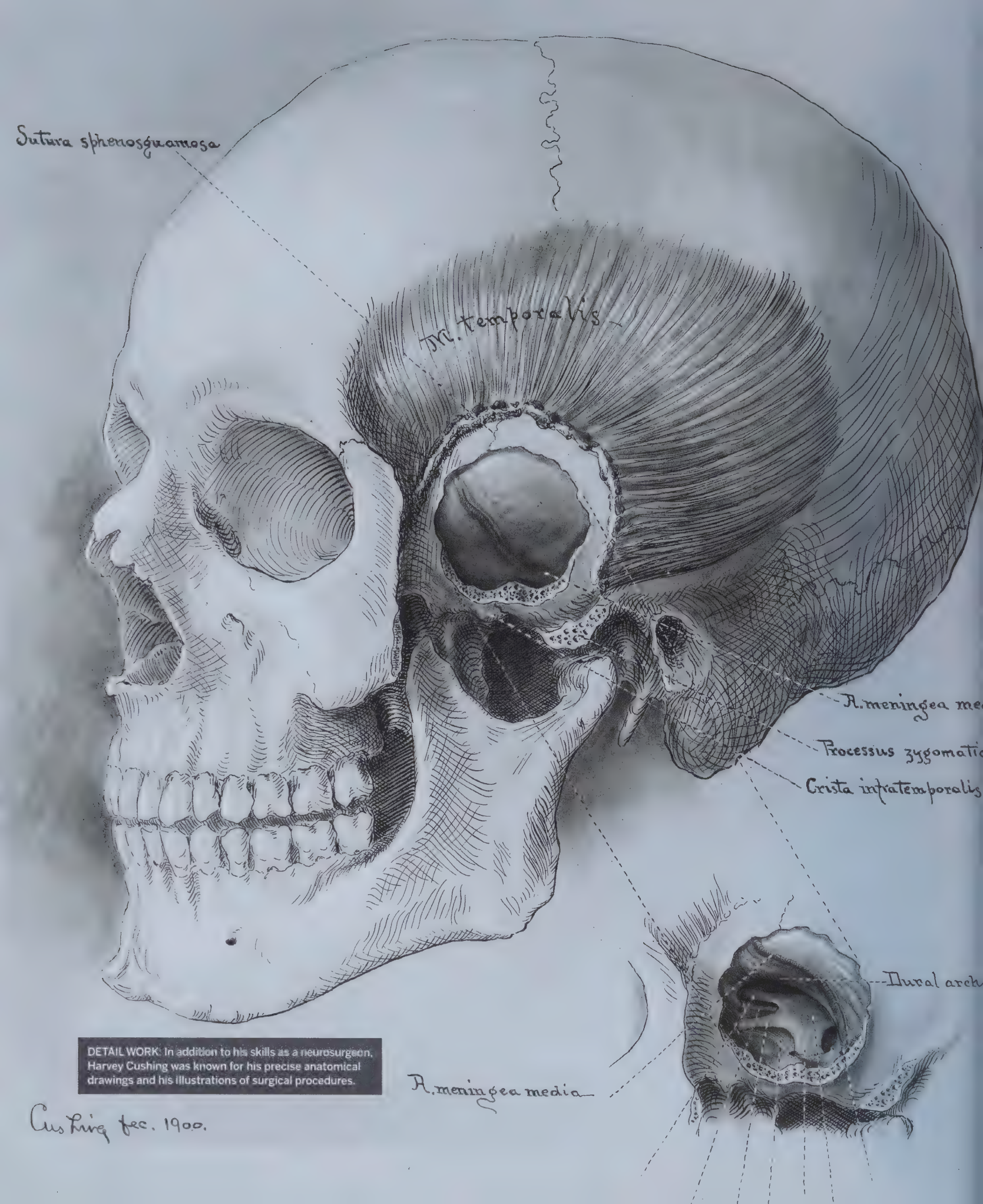
The exercise with the Etruscan sarcophagus, which comes toward the end of the Humanistic Curriculum session, is the one Martin says "almost never fails." Over the years, she's seen it unlock raw and moving stories about residents' experiences—about a wife who climbed into bed with her husband after they requested a do-not-resuscitate order, or about difficult phone calls made to family members, or the sadness of calling lawyers when the person who died had no family to notify.

By creating a space in the museum to broach these topics, the art education programs give residents permission to confront these experiences as humans, not solely as physicians, and to again get in touch with the empathy and compassion that inspired them to practice medicine in the first place.

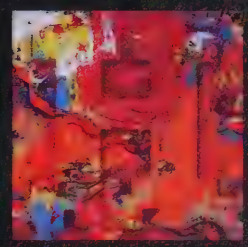
The final session in the Humanistic Curriculum takes residents into the MFA's Japanese Temple Room, a cool, dimly lit gallery with five wooden Buddhas in a meditative tableau. There, the facilitators lead the residents in a simple guided meditation.

"We talk about how, if they are going to be healers, they have to take care of themselves, too," says Martin. As much as art can deal with difficult and traumatic themes, it can also be a source of inspiration and restoration. No matter how challenging the hospital environment can be, the experiences at the museum remind new doctors that personal restoration can be found in art. ■

Michael Blanding is a Massachusetts-based writer.



DETAIL WORK: In addition to his skills as a neurosurgeon, Harvey Cushing was known for his precise anatomical drawings and his illustrations of surgical procedures.



Line Art

The work of Andreas Vesalius fascinated, and inspired, neurosurgeon Harvey Cushing

by Jeffrey Mifflin

It was to be an informal meeting, an invitation to have lunch, in fact, between the renowned neurosurgeon Harvey Cushing and Henry Viets, Class of 1916. The two were to meet in Cushing's consulting room in what was then the Peter Bent Brigham Hospital.

In his brief reminiscence of Cushing published in 1969 in the *Proceedings of the Massachusetts Historical Society*, Viets, a neurologist and medical historian, describes his lunch companion on that day in 1915.

"The surgeon had just finished an operation. ... Sitting on a high stool, he was writing up his long operative note, meticulously recording every detail and illustrating the more important procedures by clever sketches inserted at frequent intervals. These pen drawings, of considerable beauty, were designed to amplify his written descriptions in pictorial form. The writing of these notes was ... always his first task after an operation was finished and never, under any circumstances, interrupted. So intent was he at his work that even my presence only evoked a welcoming nod. ..."

Cushing, Class of 1895, was an avid collector of illustrated antiquarian medical books and a prolific author. He was also a talented artist whose lifelong hobby was to study the publications of Renaissance anatomist Andreas Vesalius. The influence that the detail and clarity of the woodcuts in Vesalian anatomical atlases had on Cushing is evident in his own commitment to preparing comprehensive, illustrated surgical notes.

At HMS, Cushing earned the first perfect grade ever given in pathology. According to certain biographers, Cushing was urged by teachers to skip further preliminary courses and focus on his work in the dissecting room, the best place for medical students to acquire hands-on knowledge of the human body. He began as a replacement house surgeon at Massachusetts General Hospital in April 1895, two months before graduation and before his formal appointment. At Mass General, he dissected amputated body parts whenever he could and performed his first full autopsies, sometimes begging grieving relatives for permission. So insistent was he that once, during a wake for a deceased patient, an irate widow screamed at him and demanded that he leave.

Rummage Sale

In 1896 Cushing took a position as assistant resident in surgery at Johns Hopkins Hospital. In Baltimore, Cushing and his wife, Katharine, lived next door to William Osler, who was himself accumulating a vast medical library. Osler often invited Cushing to inspect the latest leather-bound first editions Osler had purchased from European booksellers. Together they would pore over catalogs from British and continental book dealers and engage in animated discussions about rare books. Cushing recalled a memorable 1901 gathering at Osler's house during which he and others had the opportunity to compare five copies of Vesalius's *De Humani Corporis Fabrica* (1543). Cushing's *Life of Sir William Osler* contains myriad references to rare medical books and to Vesalius's work in particular.

Cushing acquired his first Vesalian treasure in 1903 when a colleague, after a year of studying abroad, lugged home an imperfect copy of the *Fabrica* that had been jumbled among books for sale in the back of a blacksmith's shop in a side street in Rome. Cushing's first purchase, a worn copy of what is commonly referred to as "The Paraphrasis," the thesis Vesalius prepared for his bachelor of medicine degree at the University of Louvain, arrived in 1905 at a cost of 18 marks from a dealer in Berlin.

Postoperative Procedures

Cushing left Johns Hopkins in 1912 to become Moseley Professor of Surgery at HMS and surgeon in chief at Peter Bent Brigham Hospital; he brought with him his ingrained taste for rare books and medical illustration. His notes on his surgeries and dissections, which remain at Brigham and Women's Hospital, are beautifully illustrated with heuristic drawings.

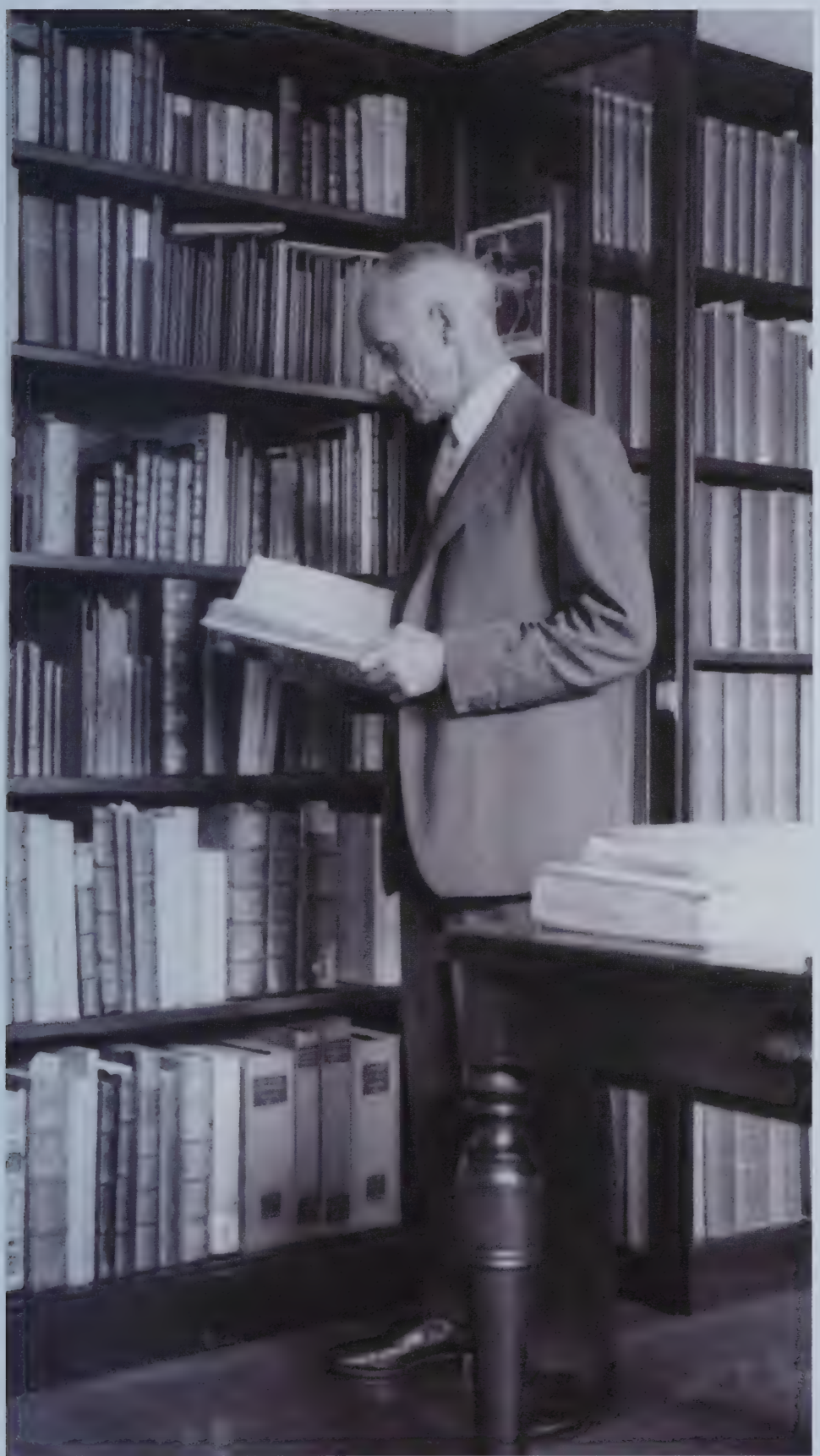
TO A T: The historiated initials in *De Humani Corporis Fabrica* show naked children, looking more wily than cherubic, variously engaged in obtaining cadavers for Renaissance anatomists, such as Vesalius. Harvey Cushing (right) was an avid collector of Vesaliana and had many of Vesalius's works in his rare books collection.

Although he was known for producing precise sketches of anatomy and his surgical procedures, Cushing employed professional illustrators for his published articles and books. One such illustrator, Mildred Codding, worked closely with him inside and outside the operating room between 1929 and 1932. In an interview in *Surgical Neurology*, Codding recalled that after operations Cushing routinely examined her sketches and drew over them to get the exact effect he wanted. The habit may well have been set by Cushing's appreciation of Vesalius's uncompromising devotion to direct observation of the human body and precise anatomical depiction.

Renaissance Man

Vesalius's study of medicine at the University of Louvain was followed by additional training at the University of Paris. While in Paris, he attended, some might argue, endured, lectures by Galenists, who read texts to their pupils from a raised seat known as the cathedra while barbers on the floor below conducted perfunctory dissections, more often on animals than on human cadavers. The precepts of ancient thinkers such as Galen had become so accepted by generations of scholastic commentators that their statements were widely considered infallible.

But Vesalius came of age when questioning tradition, whether ecclesiastical or scientific, was becoming acceptable. He sought bodies for dissection, at one point



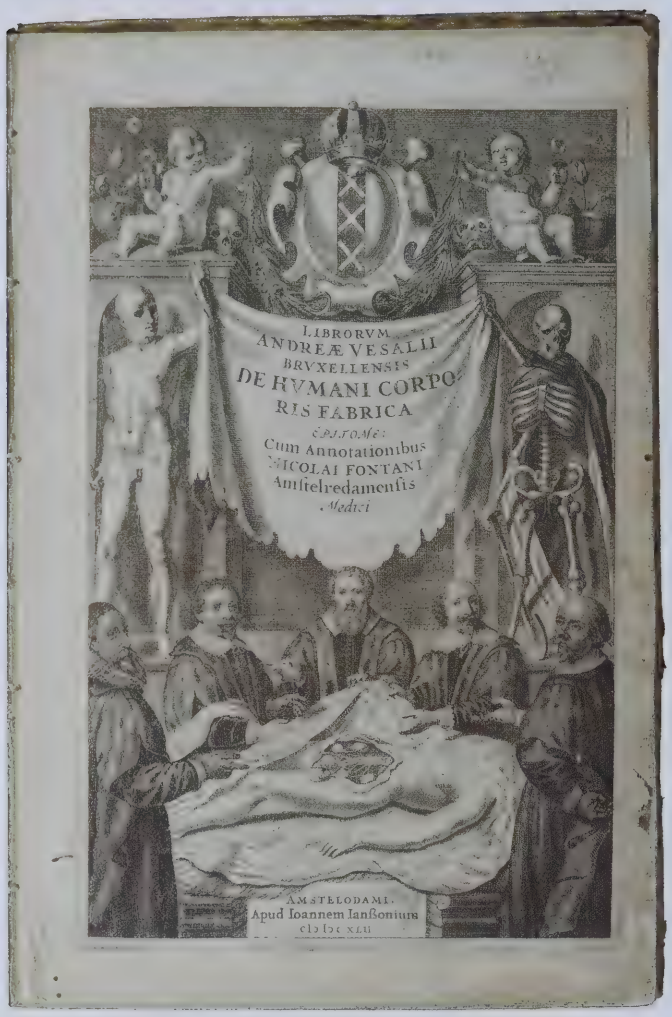
Cushing's first purchase, a worn copy of what is commonly referred to as "The Paraphrasis," arrived in 1905 at a cost of 18 marks from a dealer in Berlin.

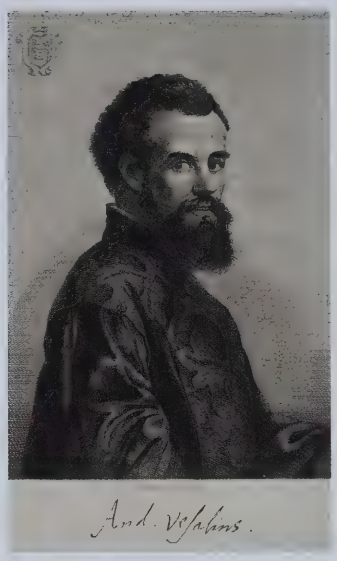
surreptitiously removing a criminal's remains from a stake on a roadside near Louvain. Midnight expeditions to Paris's Cemetery of the Innocents to dig for human bones sometimes flirted with disaster. In a story in the *Epistle on the China Root*, referenced in C. D. O'Malley's *Andreas Vesalius of Brussels*, Vesalius describes how he and a fellow student once were "gravely imperiled ... by many savage dogs," intent on the same bones. According to an anecdote in the *Fabrica*, Vesalius's knowledge of anatomy was so deep that he won bets with his uncanny ability to identify any bone by touch, even when blindfolded.

Vesalius soon sought more advantageous opportunities for anatomical investigation in Italy. At age 22, he was appointed professor of surgery at Padua, then a great seat of medical learning. The position entailed teaching anatomy. At the height of his fame some 500 spectators were said to have crowded around him during his anatomical demonstrations; cadavers were elevated by ropes to afford the audience a better view.

Many of the dissections Vesalius conducted for his anatomical illustrations, however, were performed in his home. He was known to keep cadavers in his bedroom for several weeks for intensive study and to facilitate artistic renderings. He engaged Jan van Calcar, a former pupil of Titian, to make anatomical drawings under his direction. In *Lives of the Most Excellent Painters, Sculptors, and Architects*, the sixteenth-century historian and painter Giorgio Vasari refers to van Calcar as follows: "By his hand ... were the designs for anatomical studies which the most admirable Andrea Vessalio [sic] caused to be engraved and published with his words."

Van Calcar's work is found throughout Vesalius's *Fabrica*; the frontispiece, for example, is his 1542 portrait of a 28-year-old Vesalius performing an anatomical demonstration before a throng of onlookers. The anatomical prints made from van Calcar's





BODY OF WORK: Woodcuts by Jan van Calcar, such as the frontispiece to the 1642 *De Humani Corporis Fabrica Epitome* (left), filled the *Fabrica* and the more portable *Epitome*. Above, the sixteenth-century anatomist Andreas Vesalius in an 1841 line engraving.

Cushing was able to inspect the *Fabrica*'s original wood blocks, cut after van Calcar's designs, at the University Library in Munich while on a visit to Europe.

woodcuts are precise and easily understood. Vesalius's equally precise text is keyed to the illustrations. The volume also features his historiated initials at the head of each main section. These enlarged letters are intertwined with genre art that shows the tools for dissection while also cleverly depicting the means for obtaining cadavers.

Vesalius realized that his tome was too cumbersome for medical students to carry as a reference tool—and too expensive for many of them to purchase. Consequently, he issued an *Epitome* of the full work, reduced to a selection of texts and corresponding illustrations on fourteen folio sheets. It was a great success. Cushing noted in his *A Bio-bibliography of Andreas Vesalius* that "these sheets were soon so thumbed to pieces from excessive use that a complete set of them has become more rare than the work they summarize. ..."

The *Fabrica* and the *Epitome* were revolutionary in that they recorded and disseminated anatomical facts, uniting text and illustration to show anatomical forms and the relationship of body parts to the systems in which they function. Their popularity led to many cases of plagiarism, often crudely executed. Such was Vesalius's passion for accuracy that he declared in print that he would permit plagiarists to borrow his original wood blocks to ensure that no erroneous information was published.

King Philip II of Spain persuaded Vesalius to join his court in 1559, but Vesalius left the court under mysterious circumstances to go on pilgrimage, possibly in fulfillment of a vow made while recovering from illness. Vesalius perished in 1564 on a remote Greek island after the small ship on which he had booked passage ran aground.

Artistic Pursuits

Cushing's interest in all things Vesalian took him far and wide. In 1909, with the permission of the curator of the Vesalianum at Basel, Cushing photographed a skeleton that Vesalius himself had prepared while waiting for proof sheets of the *Fabrica*. Cushing also was able to inspect the *Fabrica*'s original wood blocks, cut after van Calcar's designs, at the University Library in Munich while on a visit to Europe. The wood blocks were destroyed years later during aerial bombardments in World War II.

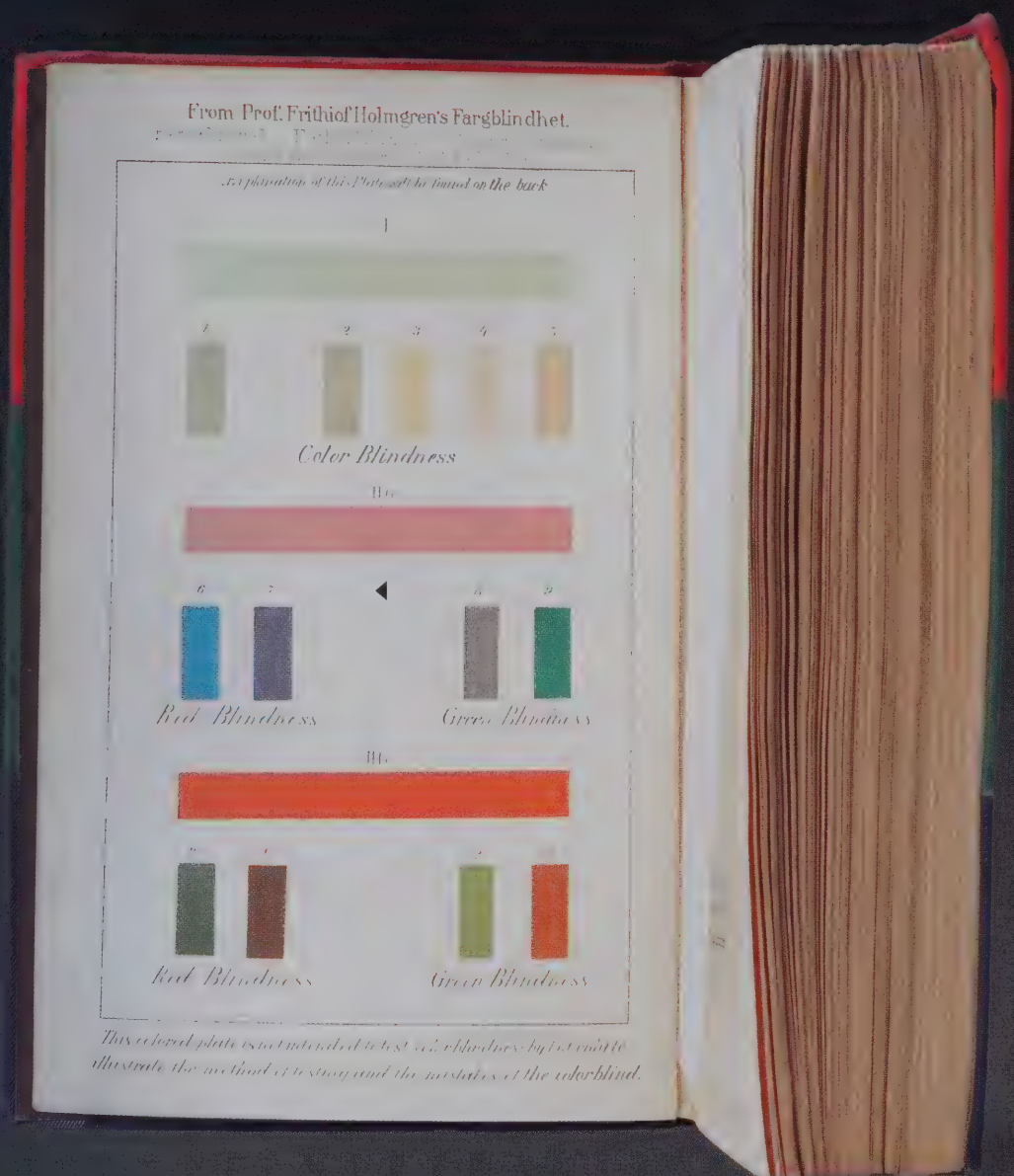
Cushing retired from HMS in 1933 to join the faculty of Yale Medical School as professor of medicine in neurology. In his recollections of encounters with Cushing, Viets describes their last meeting in 1939 during a stopover in New Haven.

"He was alone in the house, and every table, chair, and settee was piled high with books about Vesalius, for he was hard at work writing his great bio-bibliography. He pushed a few of the books from one corner and made a seat. For once ... I had to do all the talking. ... He must have felt that this was our last meeting, and so it proved to be. ..."

Cushing had experienced occasional chest pains throughout that summer but attributed them to ulcers. In early fall, he received word that Yale had found the funds and approved plans for a library to house his rare books and manuscripts. A few days later he felt serious and continuing pain after lifting a heavy Vesalian folio. He was taken to New Haven Hospital, where he died from the effects of a myocardial infarction.

A stickler for precision, Cushing remained faithful to Vesalian principles of investigation and depiction. The images incorporated in the works of Vesalius, he wrote, "spoke the universal language of art which requires no translation. ..." Cushing's *Bio-bibliography*, published posthumously, remains a landmark of bibliographical scholarship while his books on surgical techniques continue to be springboards for discussions of anatomy, pathology, or the physiology of the human body. ■

Jeffrey Mifflin is the archivist of the Massachusetts General Hospital.



Frontispiece from *Color-blindness: Its Dangers and Its Detection* by Benjamin Joy Jeffries (Boston, 1883, revised edition)

Color blindness first appeared in the medical literature in 1684, in an account of a woman who "could see very well, but no color beside black and white," by Daubeney Turberville, an oculist in England, and published in the *Philosophical Transactions of the Royal Society*.

Evidence of interest in testing for the condition surfaced later, in the mid-nineteenth century, when George Wilson, a professor in Edinburgh, noticed that some of his students could not distinguish certain colors in chemical precipitates. This revelation led Wilson to develop a test that he hoped could be used to determine fitness for occupations that relied on color preception such as painter, dyer, tailor, chemist, seaman, and railway worker.

Benjamin Joy Jeffries, Class of 1857, an ophthalmic surgeon at what was then the Massachusetts Charitable Eye and Ear Infirmary, took on the idea of occupational testing and advocated for mandatory color blindness testing in railway employees in the United States, writing that "[if] the medical, popular, and daily press would take the subject up ... the railroads would soon feel forced to act immediately in the matter."

Jeffries's 1879 book *Color Blindness: Its Dangers and Its Detection* is dedicated to his friend Frithiof Holmgren, "because I consider that to him above all others do we owe the present and future control of color-blindness on land and sea, by which life and property are safer, and the risks of travelling less."

Holmgren was a Swedish ophthalmologist who developed a test for color blindness and, as Jeffries did in the United States, strenuously advocated for mandatory testing for the condition in railway workers in Europe.

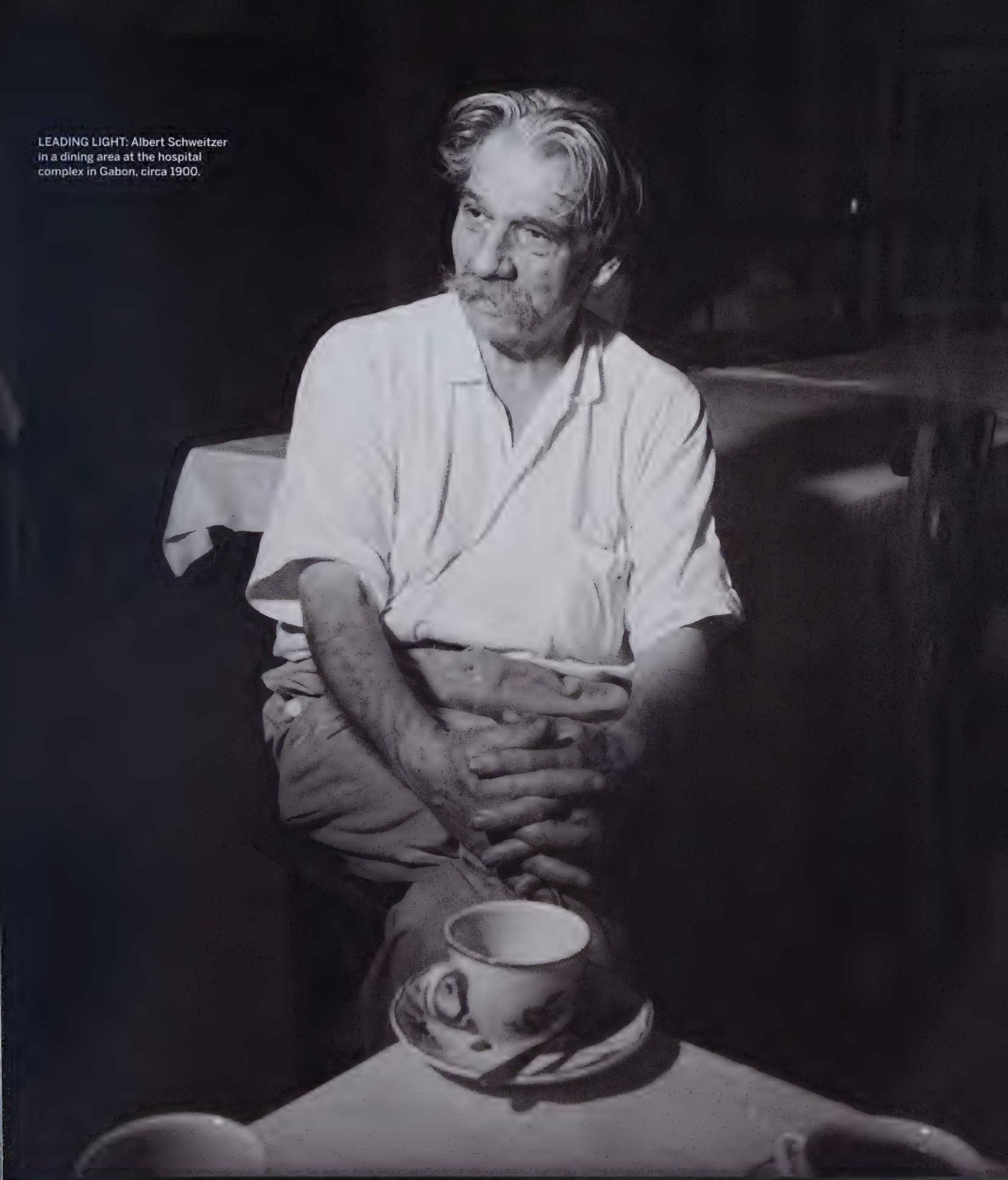
Holmgren's test wasn't the first, but it was simple, portable, and greatly reduced the amount of time needed to administer a single test. Based on the principle of comparison, the test required an individual to match a skein of woolen yarn to one in a group of colored skeins. The frontispiece from Jeffries's book, reproduced here, is a color plate of the test, which was "only intended to illustrate the characteristic mistakes of the color-blind and the colors of the sample worsteds to be employed" in the test.

—*Susan Karcz*

The imprint from serving as an Albert Schweitzer Fellow is lasting and deep

A REVERENCE FOR LIFE

by Sarah Zobel



LEADING LIGHT: Albert Schweitzer in a dining area at the hospital complex in Gabon, circa 1900.

Hospital in Lambaréné, Gabon, where Albert Schweitzer worked

With its long commitment to global and community health, it's natural that HMS would be a wellspring of Albert Schweitzer Fellows. Schweitzer is often remembered as a Nobel Prize laureate who, late in life, dedicated himself to abolishing nuclear weapons. Decades earlier, however, he was renowned worldwide as a physician who delivered medical care in areas of Africa that were bereft of such care. In 1913, with his wife, Hélène, he established his eponymous hospital in Lambaréné, Gabon.

The hospital's supporters have kept it functioning since Schweitzer's death in 1965. The Fellowship has been integral to the facility's survival.

The Lambaréné Schweitzer Fellowship Program, established in 1979, annually sends four senior medical students to the Albert Schweitzer Hospital for three-month rotations in pediatrics and internal medicine. It wasn't until 1987 that a fellow was named from a U.S. medical school other than HMS.

As fellows, HMS students experience firsthand diseases they've only read about—malaria, schistosomiasis, and intestinal parasites—but also treat more familiar conditions such as gastroenteritis, otitis media, and anemia. In addition, they learn to work effectively within the limitations of medicine in a rural area in a developing nation.

Action Figure

Before he left for Lambaréné, Samuel Stanley, Jr., '80 told a reporter that he was looking forward to the opportunity to get actively involved in patient care rather than "being the fourth person to listen to someone's heart." Little did he know how active that involvement would be: Stanley found himself in charge of the children's hospital during his first two weeks in Gabon, filling in for the chief pediatrician who had returned home to Switzerland.

"It was an extraordinary amount of responsibility for a third-year medical student," says Stanley, now president of Stony Brook University in New York and a professor of medicine in its medical school, "but it made me learn so much medicine rapidly."

He remembers one incident. A child arrived with a swollen knee joint. Stanley performed several taps to obtain fluids for testing but drew only blood. He observed that the patient's brother, who had accompanied the boy and their mother, had a bloody wad of cotton stuffed in his mouth where he'd lost a tooth. A light flipped on in Stanley's brain.

"I hadn't really thought about hemophilia because of its low incidence in Africa," he says. "I realized I had to start relying on my observational and physical exam skills, especially because we didn't have access to a lot of the standard laboratory tests."

During his time in Gabon, Stanley developed an interest in infectious diseases, fueled in part by the high incidence of malaria he saw among children at the Schweitzer Hospital.

"I realized that although we had the tools to treat malaria and make the children better, that wasn't enough," he says. "More research was needed to create a malaria vaccine or to find other ways of eradicating the malaria parasite. I realized you could help an individual patient as a physician, but if you really wanted to get into the disease problem, you had to engage in research." To that end, Stanley is currently part of a collaborative effort that has established a global health institute in Madagascar that will provide clinical assistance to the people of that island nation while also conducting health-related research worldwide.

A Nexus for Change

The entire three months that Ashaunta Anderson '06 was in Gabon, she and her colleagues at the Schweitzer Hospital were assured that vaccines were "on the way." Yet none appeared.

Before he left for Lambaréné, Samuel Stanley, Jr., told a reporter that he was looking forward to the opportunity to get actively involved in patient care rather than "being the fourth person to listen to someone's heart."

Although Anderson had experience in clinical medicine and research—she'd spent the previous year at the National Institutes of Health—until the fellowship she hadn't fully grasped how systems operate in delivering health care.

"I came to understand that health and health care delivery are much more than what we see happening in the clinic or the hospitals, or at the bench," says Anderson, who divides her time between the University of California–Riverside School of Medicine, where she's an assistant professor of pediatrics; the RAND Corporation, where she's a health policy researcher; and the clinic. "I started to have a broader perspective that included public health, policy, and government systems. I became interested in the role those entities played, and how I might engage that broader perspective to try to help more people."

Samuel Stanley

Ashaunta Anderson

"My goal is to develop a program or an intervention that would help parents and community members properly teach racial socialization to children so they can have good outcomes in both school and health."

Anderson kept a blog during her time in Gabon, documenting routine clinic days. After having seen CPR poorly executed on multiple occasions, she gave presentations on proper CPR technique, as well as on how to identify and treat hyperbilirubinemia, to physicians and the women serving as nurses.

While the fellowship reinforced a sense of service in Anderson, it also taught her that she enjoys working with other mission-oriented people, helping underserved populations, and taking positions that might be considered risky. Those characteristics are now reflected in her work at UC Riverside, a young medical school in a high-needs area that also has a shortage of physicians. She's still interested in health disparities and the social determinants of health, and, because education is one of the most consistent predictors of length and quality of life, she's also zeroed in on school readiness as a way to affect health outcomes.

"I've gone a little further upstream with both school readiness and health outcomes to look at racial socialization," she says, "which is the process by which children learn the meaning of race in society. My goal is to develop a program or an intervention that would help parents and community members properly teach racial socialization to children so they can have good outcomes in both school and health."

That First Step

According to Louise King '92, an HMS instructor in medicine at Brigham and Women's Hospital, her time as a Schweitzer Fellow served as a "stepping-off point" for her life. She followed her three months in Lambaréné with three more in what was then Zaire, working alongside her uncle, a surgeon

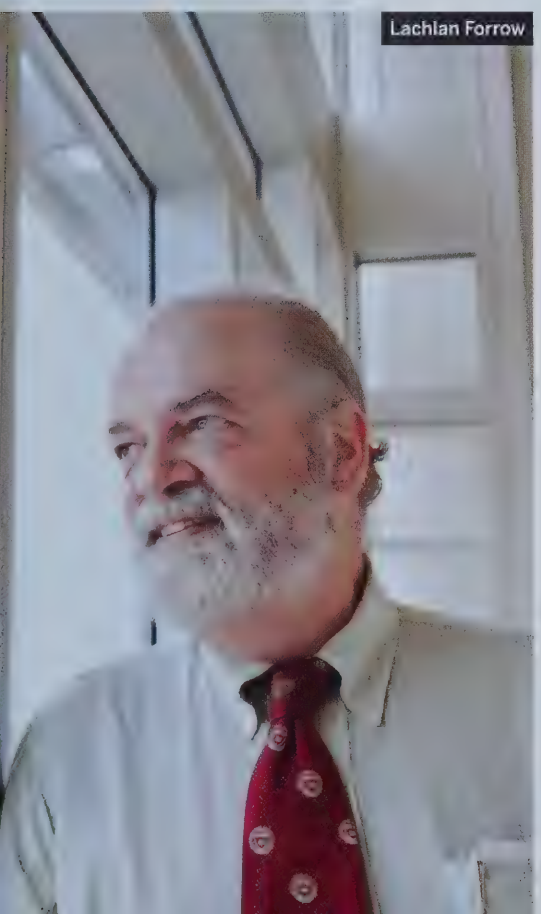
at The Good Shepherd Hospital in Tshikaji, before returning to Boston for six months of research, ultimately taking what would amount to a year's leave from medical school.

"It gave me the confidence to look for opportunities," she says, "and I realized the huge needs that are there." Although King says that during her fellowship she learned firsthand about tropical diseases including Buruli ulcer, tuberculosis, and monkeypox, her time in Gabon also allowed her to consider the broader picture of health care.

"It made a big impression on me how different the medicine was there," says King, "but it provided an important lesson on practicing medicine in a different culture."

In addition to working at the hospital, King traveled off-site with the hospital's nurses on vaccination campaigns, sometimes traveling by boat to reach patients. "It was a wonderful way to be exposed to community health delivery in the third world," she says.

Today King lives in Rwanda with her husband, Caleb King '88, and their children, seeing patients at Ruhengeri Hospital while also participating in teaching internal medicine to the hospital's family medicine residents. Through the Division of Global Health Equity at Brigham and Women's, King is working with the Rwanda Human Resources for Health program, an HMS-Rwanda partnership supported by a consortium of medical-related institutions, including Brigham and Women's and Boston Children's Hospital.


Lachlan Forrow

King's clinical work at the Ruhengeri Hospital excites her because it's providing her with an opportunity to manage a wide variety of diseases. Although she acknowledges there are some challenges to having sufficient knowledge to diagnose cardiac problems, examine peripheral blood smears, and treat rheumatoid arthritis, King also knows she is never more than a keystroke away from colleagues and specialists around the world.

A Life Altered

In the spring of 1982, Lachlan Forrow '83 and his close friend and HMS classmate Bob Ely left the United States to go "to Africa to help poor people in need." But a few weeks after their arrival, Ely drowned in a swimming accident, a tragedy that Forrow witnessed. Unsure of what he should do, Forrow contacted HMS advisors as well as friends and family; they all told him to pack up and come home.

So he stayed.

"I realized that if I went running home as soon as things got hard for me," says Forrow, "I would have proved to myself that going to Africa had never truly been about helping other people."

Forrow spent his remaining months in Lambaréné caring for patients and reflecting on "the concrete realities of human suffering." He also found himself thinking about Schweitzer and the suffering he and Hélène had witnessed, and experienced, themselves.

"Schweitzer wrote about what he called 'the Fellowship of those who bear the Mark of Pain,'" says Forrow. "The fact that sooner or later every one of us, and everyone we care about, experiences suffering is a very deep bond that connects us to each other. If we recognize that bond, maybe we can understand that this solidarity is a powerfully motivating moral basis for trying to help each other."

Forrow, who is an associate professor of medicine at HMS, director of the Ethics Programs and of Palliative Care Programs at Beth Israel Deaconess Medical Center, and president emeritus of the Albert Schweitzer Fellowship, has shepherded the fellowship's expansion to include the U.S. Schweitzer Fellowship programs. These programs, he says, expose "young health professionals to the suffering of people who have inadequate health care in ways that help them experience the fulfillment that comes from making a difference."

Translational Medicine

While in Lambaréné, Clara Jones '81 and her colleagues frequently had to choose a point in the long line of waiting patients. After that point, they would need to turn patients away, knowing that they probably had traveled far, on foot or by boat, to reach the medical center. Knowing, too, that many had been waiting all day. Jones recalls that some of the patients were there for treatment of chronic problems she had studied at HMS, such as hypertension, diabetes, and asthma. Others, however, would be diagnosed with advanced cases of cervical cancer or lymphoma, diseases that might have been prevented or treated earlier with proper screening. For Jones, witnessing what happens when people have limited access to health care has translated into a medical career focused on people in underserved urban areas.

Although Jones, like most of the Schweitzer Fellows, spoke some French before heading to Gabon, she used an interpreter while communicating with patients there, especially those who spoke only African languages. She knew it wasn't a perfect solution. Jones would ask how long a patient's problem had been active, for example, and after a lengthy, animated response, the interpreter would say: "Two years."

"You knew you were missing something!" says Jones. "All of that information, and you don't get it because you don't understand the language." Because medical records were sparse—just notes on oversized index cards—good communication with each patient was essential, especially for chronic concerns.

Achieving good patient-doctor communication has remained a concern for Jones in the years since her fellowship. As an assistant professor of public health and community medicine at the Tufts University School of Medicine and a former internist at the Dimock Center in Roxbury, Massachusetts, she's met with many Spanish-speaking patients. Although she's made a point of becoming semifluent in the language, when she conducts psychosocial interviews or wants to be sure a patient understands care details, she relies on an interpreter. Even so, she listens carefully. "There've been times I've said, 'Tell her to take this medication twice a day,' and the translator instead says twice a week. It highlights how important good communication is." ■

Sarah Zobel is a health, education, and housing writer based in Vermont.

FIVE QUESTIONS

FOR CHAO-TING WU ON GENETICS AND SPACE TRAVEL

Professor of Genetics, Harvard Medical School

What drew you to study genetics?
I was drawn to math when I was very young. I liked the exquisiteness, even the open-endedness, of the answers. Genetics is similar. It is elegant and open-ended and, like math, it's about patterns and the consequences of those patterns. Genetics allows us to use patterns to piece together our species' greatest puzzles. It can also be surprising, throwing in paradigms that we could not have guessed.

Has your research using Oligopaints affected how we understand genetics?
I think it has. I started off as a traditional geneticist, doing crosses, looking at phenotypes, and deducing from what I saw what was happening to the genome. It soon became clear that the positioning of genes in the genome and the way the genome is packaged could have a great impact on how genes function. My lab is now using fluorescently labeled, single-stranded DNA oligonucleotide probes, which we call Oligopaints, to directly visualize the genome. Excitingly, the technologies we have developed are revealing genome organization with unprecedented ease and resolution.

You're moving into areas that are relevant to space travel. Why?
There is great interest in finding ways for humans to survive the onslaught of cosmic ionizing radiation, a problem associated with long-term space travel. During space flight, astronauts can be exposed to levels of ionizing radiation that are hundreds or more times greater than those they receive on Earth, and those exposure levels will increase the farther we travel. To begin to address this issue, my lab studies ultraconserved elements, which are mysterious sequences in the genome. We have proposed that these elements may help maintain genome integrity by combating ionizing radiation's ability to create breaks in and thus to rearrange parts of the genome. In particular, we have evidence that these elements may be involved in a natural process that culls from our body those cells that have acquired deleterious breaks in their genetic material.

What do you hope to accomplish through this research?
In addition to our work on ultraconserved elements, I am interested in understanding how the biology of plants and animals responds to the absence of gravity and then applying that knowledge to make it safer for humans and other organisms to live in space. For example, my group will be using Oligopaints to visualize the effects that being in outer space may have on the genome. Ultimately, how we survive in space is going to depend to a great extent on our genome.

What are some of the more rewarding aspects of your research?
One of the more rewarding aspects of doing any research is making discoveries. Indeed, for me, research is more than being correct; it's about learning something new, even if mistakes are made along the way. When I was a student, I thought there was nothing more exciting than carrying out an experiment that would lead to new insights. But now, watching my students, postdocs, and assistants make discoveries—well, that is far more rewarding. *—Savannah Young*

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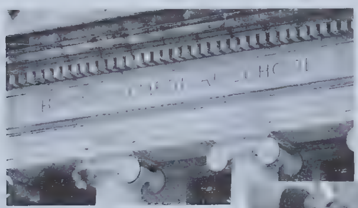

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M1623

DO NOT WRITE BELOW THIS LINE

President's Report

The Alumni Council's October meeting was quite a busy one.

The MAVEN project gave us an update on its use of telehealth and alumni to consult in underserved areas of the country. Reports on the student online publications, *Harvard Medical Student Review* and *Thirdspace*, showed they complement each other—and decidedly compliment HMS. Following Dean Flier's report to us regarding the School's first executive education course with Google and Apple, there was a suggestion from Phil Landrigan '67 to explore methods of monetizing HMS educational pursuits.

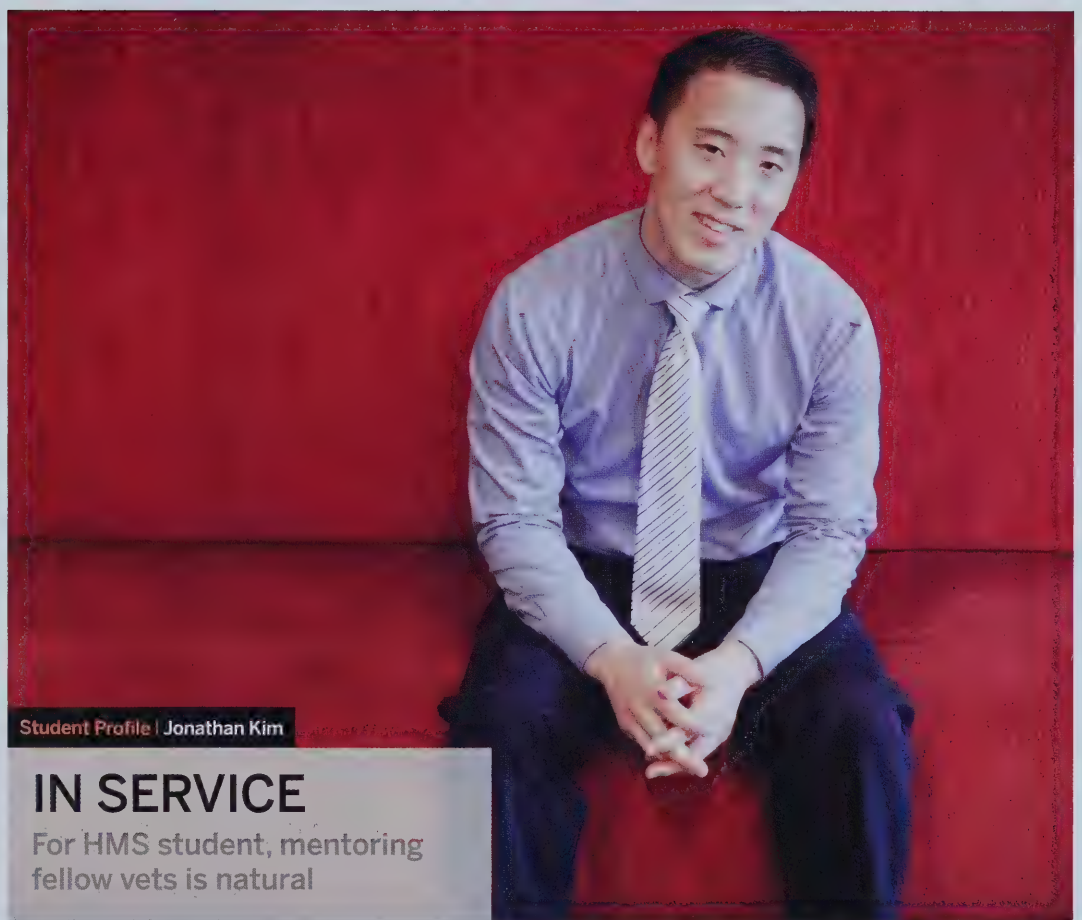
With so much change afoot, and so much talent residing in the Council, Barbara McNeil '66 suggested, and Council members solidly agreed, that the Council should promote subcommittees to work on various initiatives between its meetings. These subcommittees could tackle such issues as lessening student debt, researching discounts on CME courses for alumni, developing the listserve initiative, promoting global use of the School's external education program, and expanding access to electronic journals.

Finally, and just as importantly, Carolyn Walsh '09 leads a project to reach out to fourth-year students as they move to residencies.

I welcome your thoughts and suggestions.

Michael LaCombe '68 is a cardiologist at Maine General Medical Center and professor of medicine and medical humanities at the University of New England.

COURTESY OF MICHAEL LACOMBE



Student Profile | Jonathan Kim

IN SERVICE

For HMS student, mentoring fellow vets is natural

LOOKING BACK, first-generation Korean-American Jonathan Yong Kim '16 knows he would have gone into medicine eventually. But his childhood aspiration was to grow up to be a soldier. In high school, when he heard about the U.S. Navy SEALS, an elite military special operations unit, he knew that's what he wanted to become. At the time, he says, he didn't realize it would lead him to his true calling.

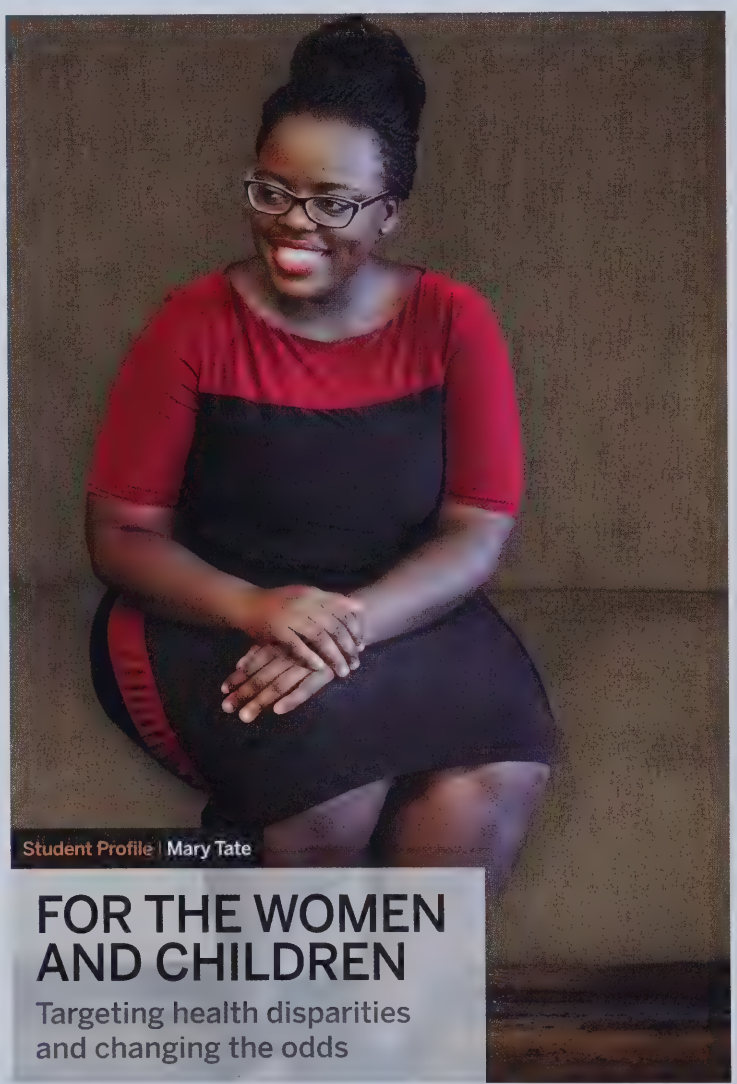
After high school, Kim served for seven years as a Navy SEAL, specializing in trauma medicine during two tours of duty in Iraq. While in Iraq, he earned a Bronze Star for saving a wounded fellow service member and a Silver Star for saving the life of a wounded Iraqi soldier. As a medic, or corpsman in Navy terminology, his role was to stabilize the injured until they could receive a higher level of care.

It was in a combat hospital where he watched the military surgeons save lives that Kim says he became inspired to become a physician. With help from military benefits and scholarships, Kim attended the University of San Diego and is now a fourth-year student at HMS, planning to go into emergency medicine.

Kim is currently mentoring fellow veterans and is passionate about helping veterans who want to get into medical school. He hopes to do more mentoring and recently joined Service to School, a nonprofit founded by veterans with the mission of helping vets gain admission to college and graduate school. Kim says he would like to spend more time in the future addressing veterans' health care issues.

"I know of service members who have fallen through the cracks of our health care system," Kim says. "As a fellow service member, I am committed to reducing these disparities so our veterans can receive the care they deserve."

—Bobbie Collins



Student Profile | Mary Tate

FOR THE WOMEN AND CHILDREN

Targeting health disparities and changing the odds

MARY TATE '17 knew she wanted to be an obstetrician long before she could spell the word.

Tate recalls how, as a college student, she was shocked to learn that infant mortality rates in her home state were four times higher among Blacks than among their Caucasian counterparts.

Eventually, the interest she had as a young girl in becoming an obstetrician grew into a young woman's conviction that she might be able, someday, to change those odds.

"What I'm passionate about," says Tate, "and what I want to do in my future, is to work to reduce racial and ethnic health disparities in infant mortality."

After graduating from Dartmouth College, Tate won a fellowship to work with One Heart World-Wide, a nonprofit organization whose mission is to improve maternal and neonatal health in remote areas of the world.

During that fellowship, Tate came to appreciate the power that community health workers had to influence health outcomes and began thinking about how to employ that concept in the United States.

Two months after arriving at HMS, Tate cofounded MOMS—Medical Students Offering Maternal Support—a program that matches medical students with pregnant women at community health centers for months-long relationships.

With the support of the Center for Primary Care at HMS, this program, which started at the Bowdoin Street Health Center in Dorchester, is being expanded in collaboration with the child and family services program at the Dimock Center in Roxbury, both of which serve people in Boston neighborhoods where infant mortality rates have fallen but still remain higher than in more affluent areas.

Because Tate wants to know that the methods being used in MOMS are as effective as she thinks they are, following her third year she plans to apply to a master of public health program "to better prepare myself for the kind of research that I'm interested in now."

—Elizabeth Cooney

Curbside Care

Meeting patients where they live is key to providing better health for vulnerable populations

He was known as a "frequent flyer," a regular visitor to emergency departments and urgent care clinics who consistently failed to manage his diabetes. Living in Boston, he was close to some of the best medical care anywhere, but his illness remained out of control.

At first, the patient's repeated bouts of illness mystified Monica Bharel, an HMS instructor in medicine at Massachusetts General Hospital and commissioner of the Massachusetts Department of Public Health, but as she learned more about the man's life, the mystery was solved. One key issue was the fact that he was homeless.

Bharel, who went on to serve as chief medical officer for the Boston Health Care for the Homeless program, spoke about the challenges of caring for the most vulnerable patients at a seminar hosted by the HMS Department of Global Health and Social Medicine and the School's Center for Primary Care. She was joined by James O'Connell '82, an HMS assistant professor of medicine and founder and president of the Boston Health Care for the Homeless Program, and Paul Farmer '88, the Kolokotrones University Professor of Global Health and Social Medicine and head of the HMS Department of Global Health and Social Medicine.

"People's stories matter," Bharel told attendees. "We know so much about the pathophysiology of diseases, but we know so much less about where a man should store his insulin when he sleeps under a bridge."

The speakers agreed that building personal relationships with individuals and communities is the foundation for providing excellent care.

"It's about learning who you are serving and what they want," O'Connell said, noting that homeless programs around the country all look different because different communities have different needs.

Farmer noted that one difference between health care work in places like Boston and in nations without existing health care systems is that in the latter, spending on health and education hovers near zero.

"The first thing we need to do in nations without good systems is let costs soar," Farmer said, not only because money is needed to deliver better health care, but because investments in health and education yield immense dividends in economic growth.

The speakers felt that the work of treating vulnerable patients was not only morally necessary but richly rewarding.

"Caring for poor people—whether they are in another country or living within the shadows of this campus—is a challenge requiring great creativity," O'Connell said. "That's the real work of places like HMS."

—Jake Miller

Student Profile | Carlos Estrada Alamo

Journey of Hope

A formerly undocumented immigrant charts a course to change the trajectory of health care

WHEN HE WAS FIVE YEARS OLD, Carlos Estrada Alamo '17 traveled with his family from his native Guanajuato, Mexico, to Seattle, Washington. His family arrived filled with hope for the future in the land of opportunity, but without the benefit of immigration documents.

"I've always had to find ways to navigate through, over, or under the challenges in front of me," Estrada says. Instead of stopping when things got tough, he simply found other ways around the obstacles in his path.

Growing up, Estrada had seen that limited access to health care and a fear of interacting with the health care system were barriers to greater opportunity for many immigrant families. He saw this firsthand while working in a community hospital.

"People would come in with complicated chronic conditions with roots in their social and economic histories, but the care we could provide just treated the most superficial symptoms," he says. "We weren't doing anything to change the trajectory of their health."

Estrada came to HMS with a recently acquired permanent resident status, sponsored by his wife. He was seeking a place where he could work with and learn from people who are focused on the wider view. To support his studies, Estrada received a 2014 Paul & Daisy Soros Fellowship for New Americans.

The challenges of learning the basic science and clinical skills necessary to become a physician is daunting even without the additional layer of trying to understand the intricacies of economics and human systems, says Estrada.

"We're so focused on microscopic details, yet you also need to see how the pieces fit together so you don't lose sight of the question that matters the most," he says, "which is how do we best preserve our body—this fragile biological machine—in order to live life to the fullest."

—Jake Miller

Peaks and Valleys

The unsettling nature of being a new president

JUST WHEN YOU BEGIN to feel you've arrived, that you've achieved a degree of stature, it happens. You get elected by your peers to an office, sit at the head of a table, and receive a cardboard folder with your name it. Everybody else gets just a stack of papers.

You don't get an agenda for the meeting. You receive a briefing. Several briefings, in fact. There are items in black for your information and items in red that you had better say. There are no highlighted items about things you'd better not say.

Around the table are important people. Because it's clear that they all have arrived, it helps you believe that you have, too. You become a little less unnerved.

The very first female-full-professor-in-the-history-of-the-medical-school hugs you. You wonder if that gives you cachet, whether you should act with panache, or whether one causes the other.

You get through the meeting, go to the dinner, and sit across from an invited guest, a second-year medical student. You look forward to a relaxing conversation.

He calls you Mr. President and restores some of your uppity-ness. Then, in response to your question, he tells you he's working on a subatomic cure for all forms of cancer, plays a Bach cello suite to relax while working on the unified field theory, and studies Finnish and Hungarian during his commutes on the "T."

He adds, "I've also been tutoring a couple of first-years."

Then he smiles sheepishly. "It's just amazing how much they know."

—Michael LaCombe

Michael LaCombe, president of the School's Alumni Council

CLASS NOTES

NEWS FROM ALUMNI

1945

Giulio D'Angio

We had a fine family reunion in Bermuda in August, around the 60th anniversary of my having first visited there. My great-granddaughter Maggie was among the fifth generation of D'Angios to walk those sands. I am co-authoring a history of the International Society of Pediatric Oncology, of which I was once president. My remarkable wife, Audrey Evans, continues, even now at age 90, to receive awards and medals for her many philanthropic and professional achievements.

I saw **George Hill '57** at the Philadelphia Club in November, at an event where my wife was being honored with an award from the Colonial Society of Pennsylvania. The award recognizes her work in furthering the welfare of the greater Philadelphia community, particularly by founding Ronald McDonald houses and the St. James School for underserved children.

1957

Wilbert Aronow

I have edited my thirteenth book, *Translational Research in Coronary Artery Disease: Pathophysiology to Treatment*, which was published by Elsevier in November.

Stephen Friedland

Still keeping a distal phalanx in medicine as chair of the Vassar Brothers Medical Center Ethics Committee and otherwise enjoying retirement. Our family, fortunately, is doing well, and all four grandchildren have now finished high school.

1959

Alan Friedman

My classmate **Thomas Kuhns** and I have been practicing ophthalmology together for fifty years and still enjoy it. We look forward to many more years of sharing this wonderful association in New York City.

1966 50th REUNION

Dennis Bauman

I am still working part-time in Elkin, a small town in North Carolina. My wife and I enjoy the pace of life, cost of living, and natural beauty of this area. I am biking six and a half miles per day and golfing fairly regularly. I feel blessed.

1974

Edmond Raker

After deciding to retire this coming July, I've realized I will find it very hard to give up doing vascular surgery. It is an intricate and delightful specialty. Now I must search for what else to do.

CLASS NOTES

NEWS FROM ALUMNI

1983

Robert Olvera

Last year, our daughter Emily Rose lost her seventeen-year battle with acute lymphoblastic leukemia. She was twenty four. I was an advocate for the aid-in-dying movement in California and helped the state become one of five with a law allowing aid in dying.

1988

Margaret Chaplin

Michael (Aronow) and I continue to be happily married. Our kids are rapidly leaving home, however, with our oldest, Ben, now in medical school at the University of Connecticut. In addition to my work as an addiction psychiatrist, I am coaching high school lacrosse.

2003

Vasant Narasimhan

I am humbled by my recent election to the National Academy of Medicine and by being named one of *Fortune* magazine's "40 Under 40" for 2015. The teams I have worked with share all the credit, along with my wife, Srishti (Gupta). The vaccines and medicines we have developed will, we hope, improve and protect the lives of millions of people around the world. I am looking forward to the road ahead and finding more medicines to help make longer and better lives possible.

2015

Gilad Evrony

I was honored to be named one of *MIT Technology Review*'s "35 Innovators Under 35." This recognition is for the neurogenetics technologies I helped develop in the laboratory of Christopher Walsh at Boston Children's Hospital. I'm looking forward to continuing to contribute to the increasingly broad efforts of the scientific community to develop new neurotechnologies to understand how the brain develops and functions in health and disease.

Share Your News

If you have updates you'd like to share in Class Notes, you can submit them easily and securely to classnotes@hms.harvard.edu. Be sure to include your full name and class year.

OBITUARIES

REMEMBERING DISTINGUISHED LIVES

1930s

1939

William T. Carleton
December 31, 2015

1940s

1940

Charles P. Haseltine
November 27, 2015

1942

Allan D. Callow
December 22, 2015

Herbert D. Lewis
November 10, 2015

1943

John A. Flick
October 26, 2015

1944

Frederic P. Herter
November 7, 2015

1946

Willard Dalrymple
October 5, 2015

1947

John A. Duggan
October 8, 2015

John H. Monroe
January 12, 2016

William J. Porell
November 19, 2015

1948

Edward E. Callaghan
September 12, 2015

1950s

1950

Richard L. Smythe
November 20, 2015

1953

Marshall B. Allen, Jr.
November 13, 2015

Robert G. Fletcher
October 19, 2015

Frederik C. Hansen, Jr.
August 23, 2015

1954

Edward J. Budil
November 16, 2015

William Kornfeld
July 14, 2015

1956

Everett W. Haggett
November 25, 2015

Russell A. Rohde
July 7, 2015

Arnold N. Weinberg
September 28, 2015

1960s

1962

Bernard D. Kosowsky
November 19, 2015

1963

J. R. Saphir
August 30, 2015

1970s

1976

Brent A. Oldham
December 21, 2015

1990s

1994

Vanessa D. Smith
December 11, 2015

This listing of deceased alumni includes those alumni whose notices of death were received between September 26, 2015, and January 22, 2016. Links to full obituaries of these alumni can be found at hms.harvard.edu/memoriam.

If you know of an HMS alumna/us who has died recently, please email the link to the obituary to hmsalum@hms.harvard.edu.

TAKING A HISTORY

PROFILE OF MICHELLE RIVERA, CLASS OF 1992

CLAIM TO FAME

Radiologist specializing in breast imaging, Mecklenberg Radiology Associates, Charlotte, North Carolina

ROOTS AND BRANCHES

"My father died on Christmas Day," says Michelle Rivera '92, "when I was eleven years old. He had been sick for a short time, but my parents didn't understand what the doctor was telling them and didn't know what was going on."

After her father's death, Rivera vowed to be better prepared for family health crises; she decided to become a doctor. Later, she realized that it was also the complexity of medicine that attracted her. Medicine required a lot of science but also a lot of critical thinking and creativity.

With their father and husband gone, Rivera and her mother found themselves "plunged into pretty desperate economic times." Yet she grew up secure in the knowledge that her mother believed in Rivera's career dream and that "she would be willing to give everything up to pay for my education." For her part, Rivera believed that she could thank her mother best by getting good grades and getting into medical school. Her strategy worked: She was accepted into HMS.

WAYS OF SEEING

While at HMS, Rivera selected radiology as her specialty. It attracted her because it was where all the new technologies were coming from, guaranteeing Rivera a career in which she would be "always learning something new."

Rivera's expectations for her chosen path have been more than met. She loves her work, despite the intense emotions that it can trigger. When delivering good news, such as a negative result on a cancer screen, there are waves of relief and gratitude to deal with. And when she must deliver bad news, "the tears are real, and the tears of the family are real. You know what lies ahead for the patient."

Although it wasn't a conscious decision to find an outlet for these emotions, Rivera found one in painting. She came to fine art gradually. While she was an undergraduate at Columbia University in New York City, Rivera loved looking at the Impressionist paintings in the Metropolitan Museum of Art. But she didn't start painting herself until about ten years ago, when she started taking classes.

Painting, Rivera says, brings her physical joy. "It's all about moving the paint on the canvas. I paint at an almost frenetic pace, because I just want to transfer all my energy onto the canvas."

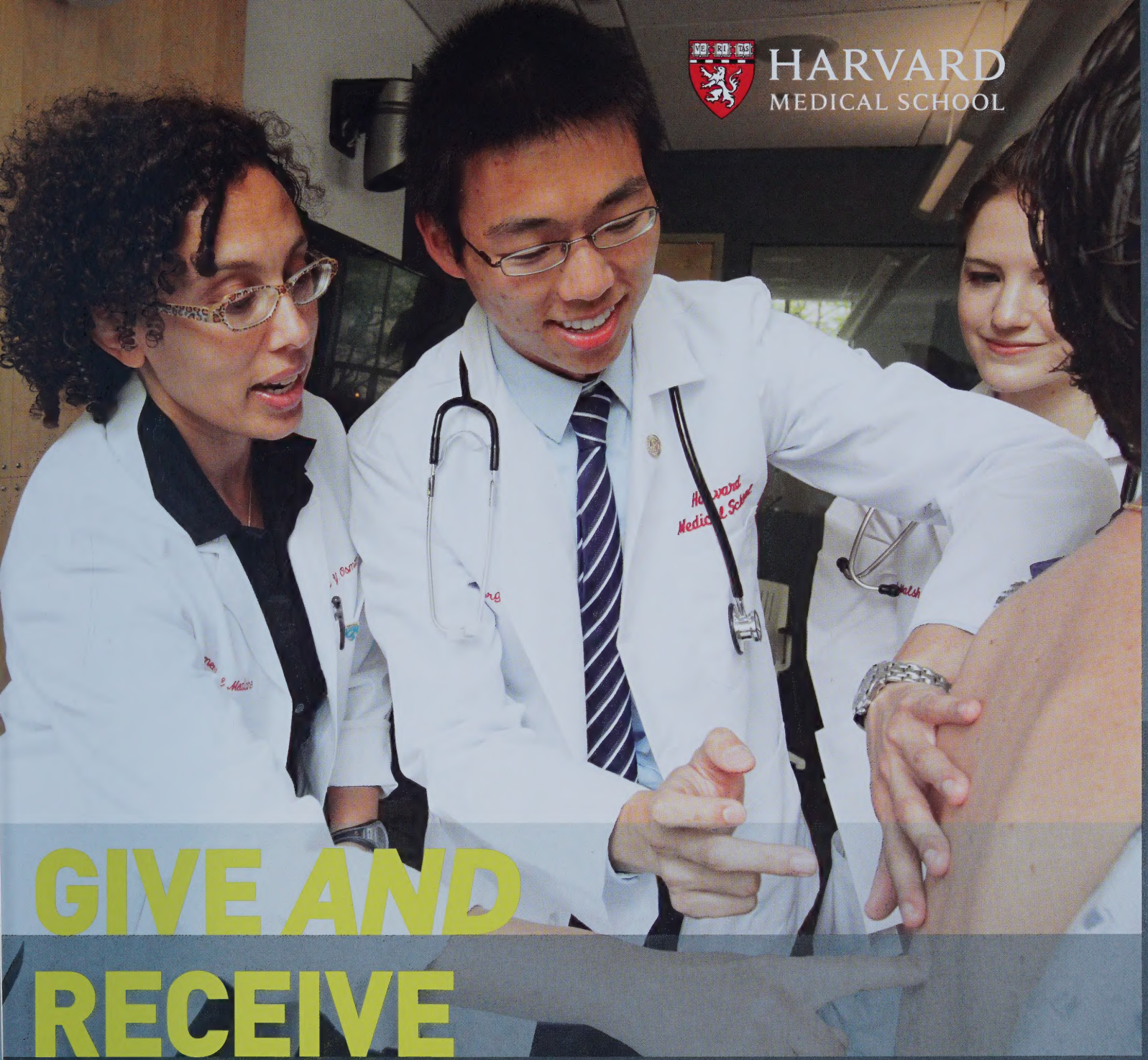
A THING OF BEAUTY, A JOY FOREVER

Rivera's twin vocations complement each other well. The world of breast imaging is tightly rule-driven: "There are rights, and there are wrongs," she says, along with a highly specific lexicon and a complex coding system for imaging findings.

"On the other hand, when I paint," she says, "it's my world. And the rules are the rules that I make."

Rivera sees her art as a lifetime skill. She admits that when she is eighty years old she may no longer be able to read a mammogram, but she will be able to paint. And in the meantime, she has something she loves to provide an outlet for stress and just add a dimension of joy to her life.

—Susan Karcz



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